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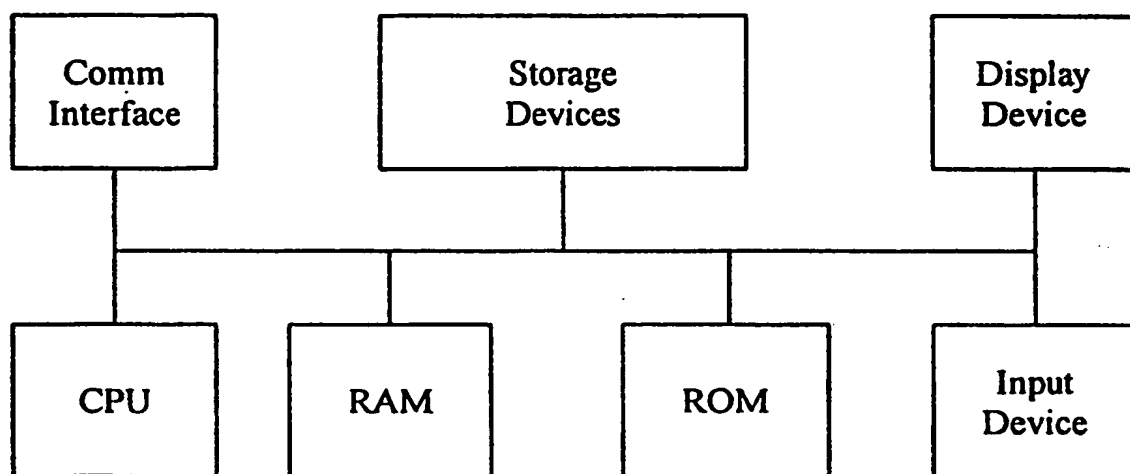


FIG. 1A

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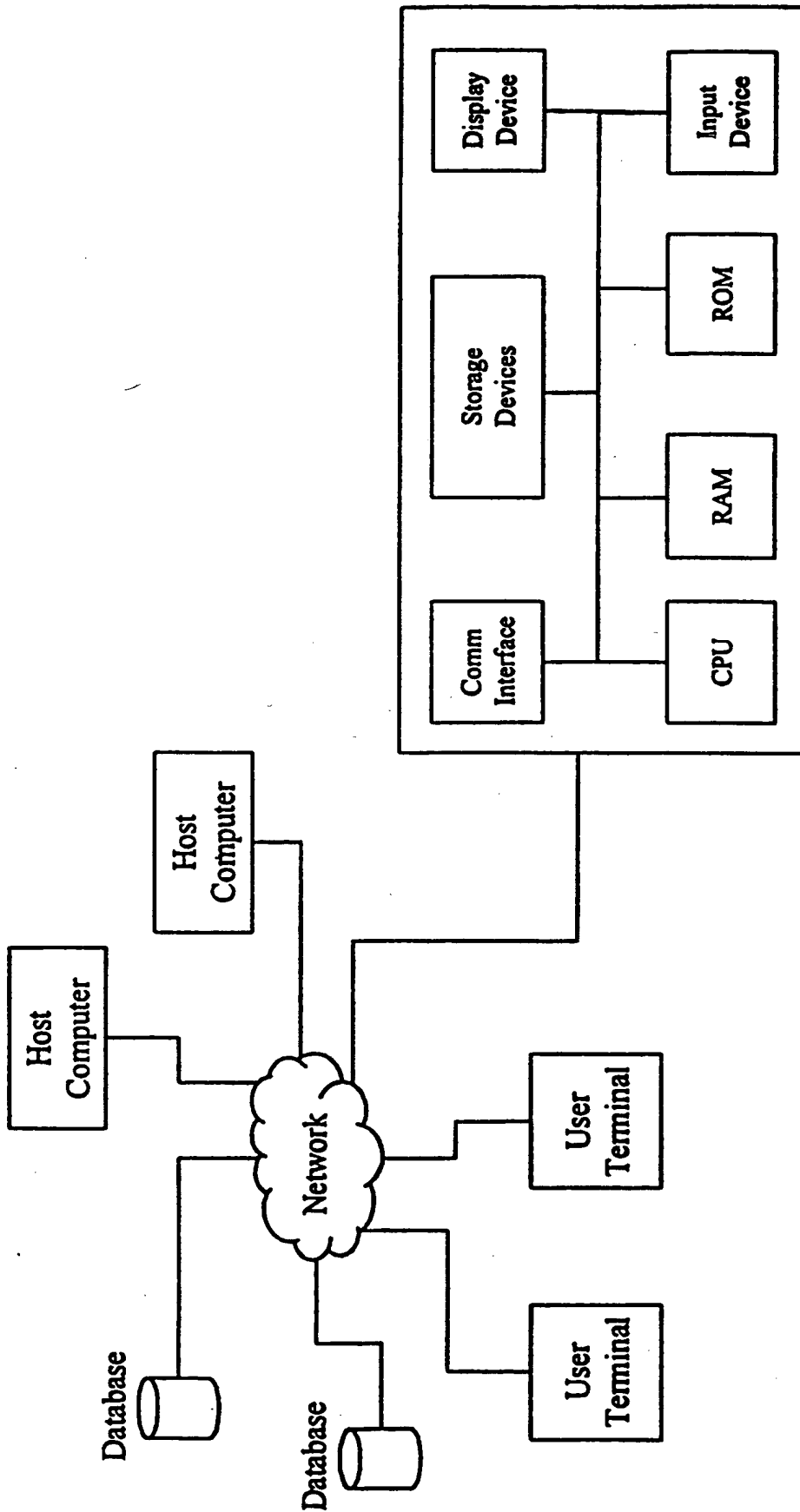
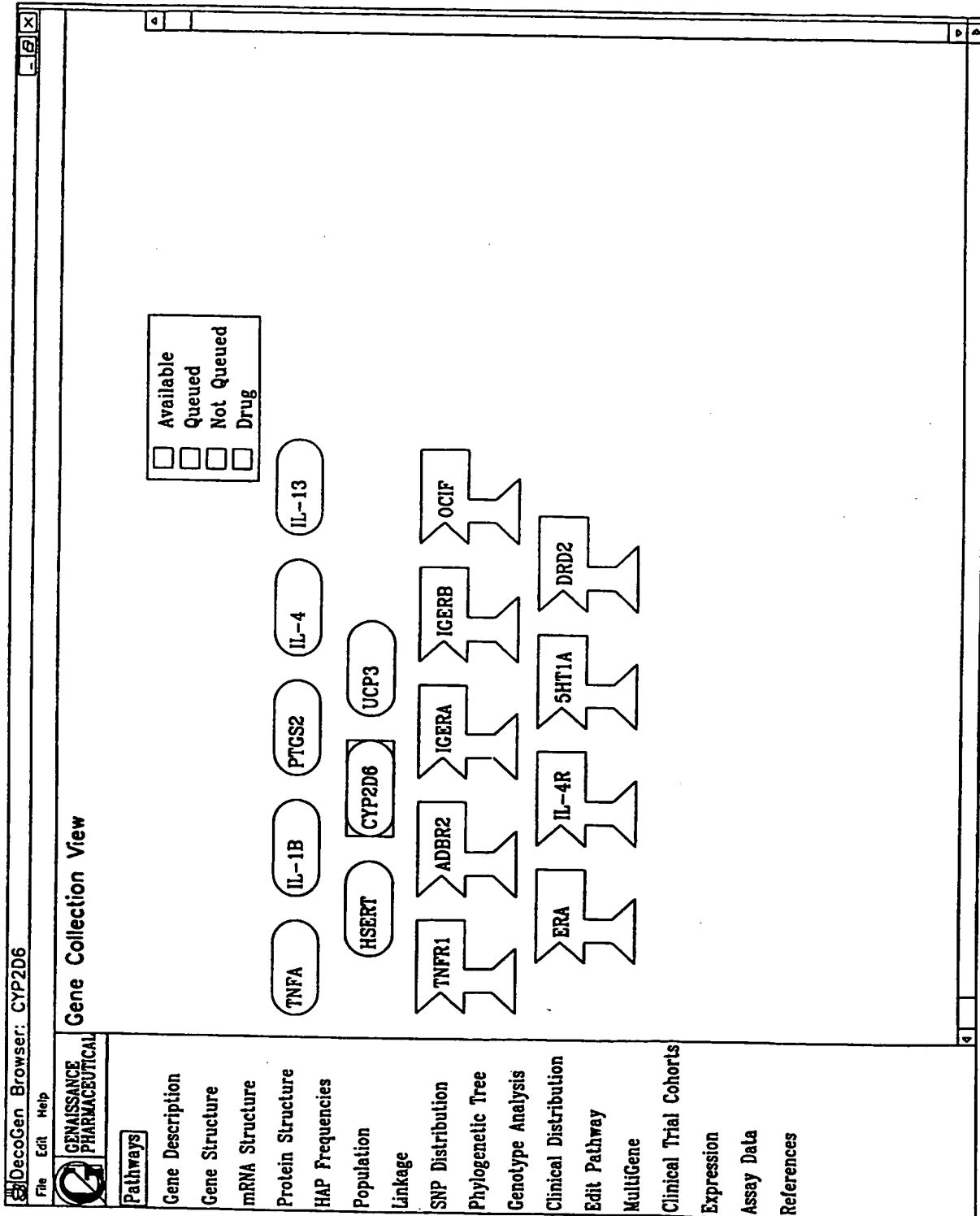


FIG. 1B

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FIG. 2



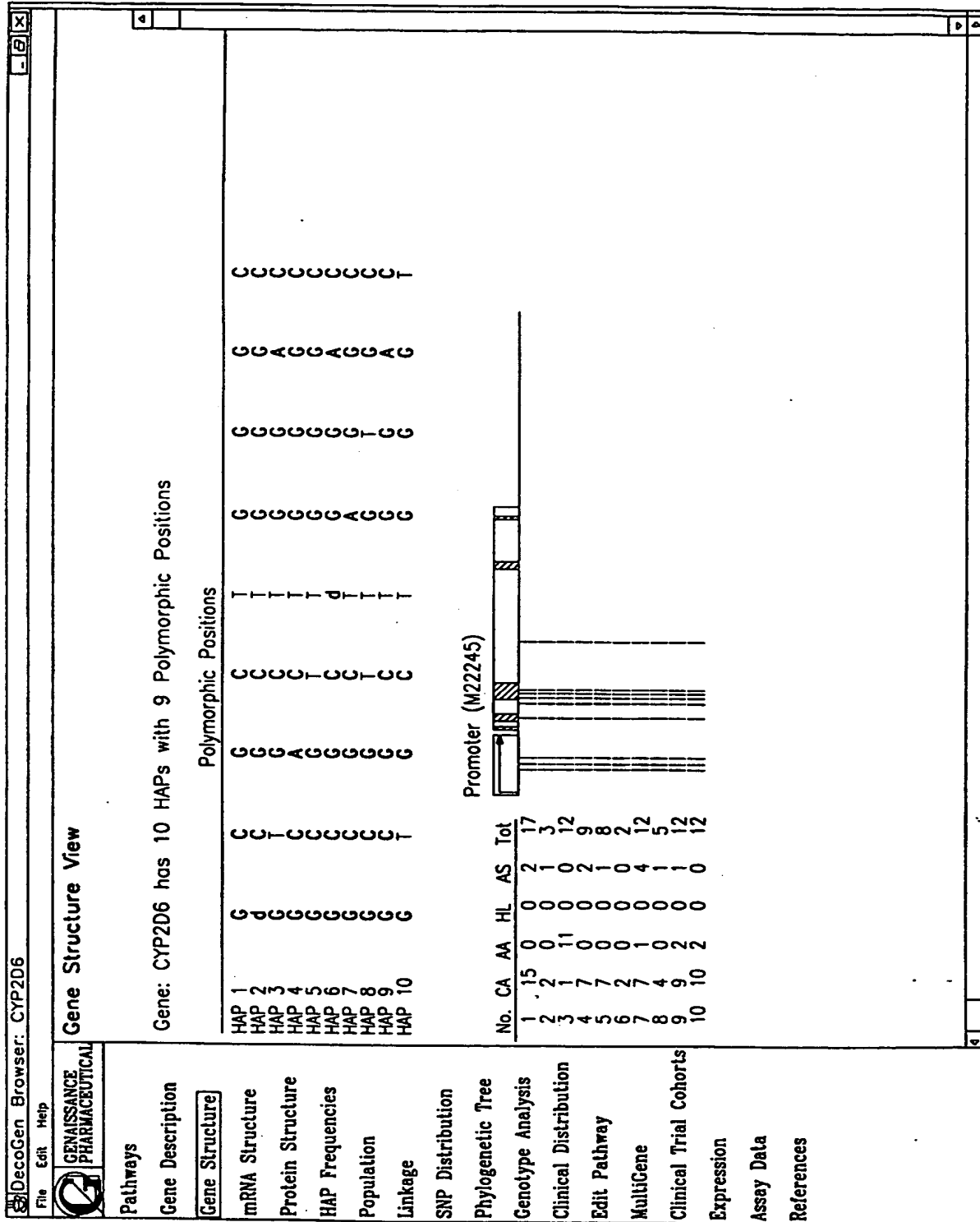
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FIG. 3

DecoGen Browser: CYP2D6																					
File Edit Help																					
GENAISSANCE PHARMACEUTICAL																					
Pathways	Gene Description View																				
Gene Description																					
Gene Structure																					
mRNA Structure																					
Protein Structure																					
HAP Frequencies																					
Population																					
Linkage																					
SNP Distribution																					
Phylogenetic Tree																					
Genotype Analysis																					
Clinical Distribution																					
Edit Pathway																					
MultiGene																					
Clinical Trial Cohorts																					
Expression																					
Assay Data																					
References																					
	<table> <tr> <td>Name</td><td>CYP2D6</td></tr> <tr> <td>Definition</td><td>Human cytochrome P450 IID6 (CYP2D6) gene</td></tr> <tr> <td>Function</td><td>Metabolic enzyme</td></tr> <tr> <td>Organism</td><td>Homo Sapiens</td></tr> <tr> <td>Length</td><td>9432</td></tr> <tr> <td>No Features</td><td>13</td></tr> <tr> <td>Population Size</td><td>46</td></tr> <tr> <td>No. Haplotypes</td><td>10</td></tr> <tr> <td>Nucleotide Polymorphism (theta)</td><td>5.6E-4 +/- 3.1E-4</td></tr> <tr> <td>Nucleotide Diversity (pi)</td><td>2.8E-4 +/- 1.8E-4</td></tr> </table>	Name	CYP2D6	Definition	Human cytochrome P450 IID6 (CYP2D6) gene	Function	Metabolic enzyme	Organism	Homo Sapiens	Length	9432	No Features	13	Population Size	46	No. Haplotypes	10	Nucleotide Polymorphism (theta)	5.6E-4 +/- 3.1E-4	Nucleotide Diversity (pi)	2.8E-4 +/- 1.8E-4
Name	CYP2D6																				
Definition	Human cytochrome P450 IID6 (CYP2D6) gene																				
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No. Haplotypes	10																				
Nucleotide Polymorphism (theta)	5.6E-4 +/- 3.1E-4																				
Nucleotide Diversity (pi)	2.8E-4 +/- 1.8E-4																				

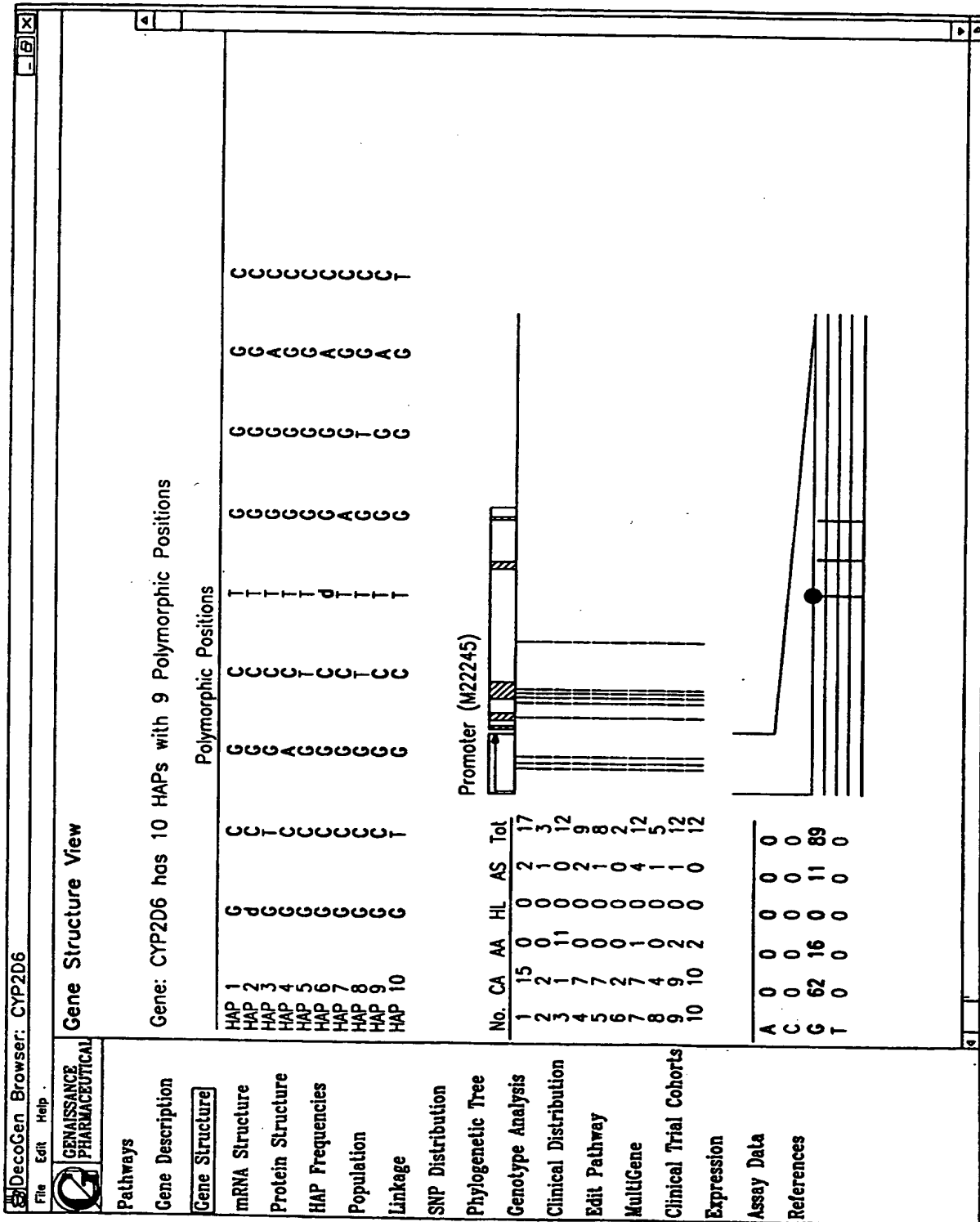
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FIG. 4a



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FIG. 4b



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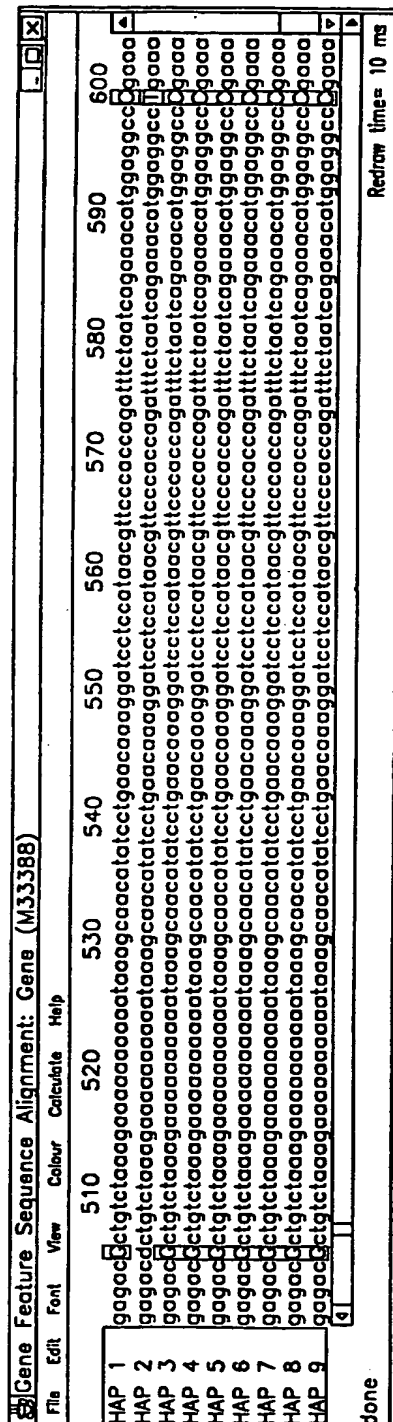
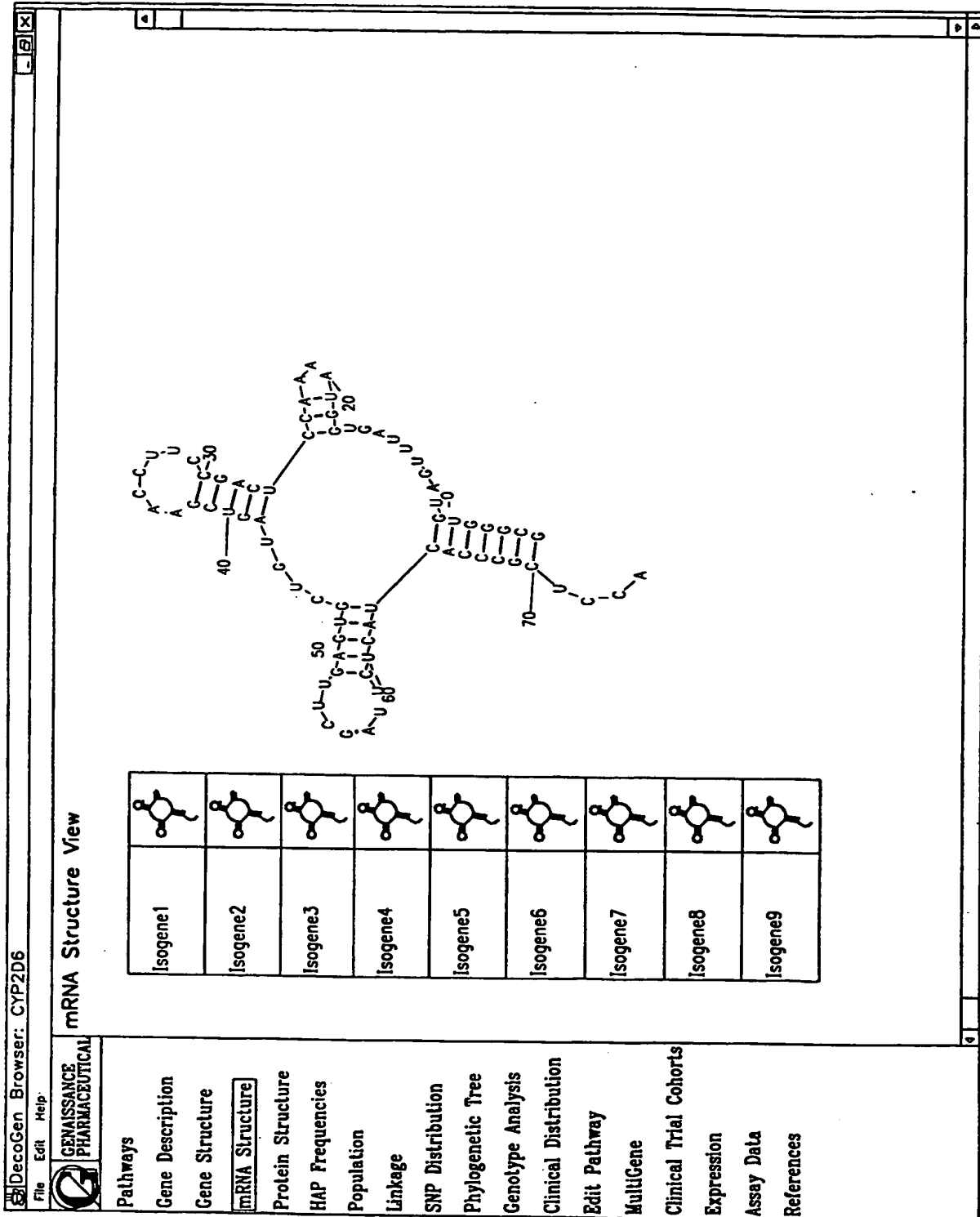


FIG. 5

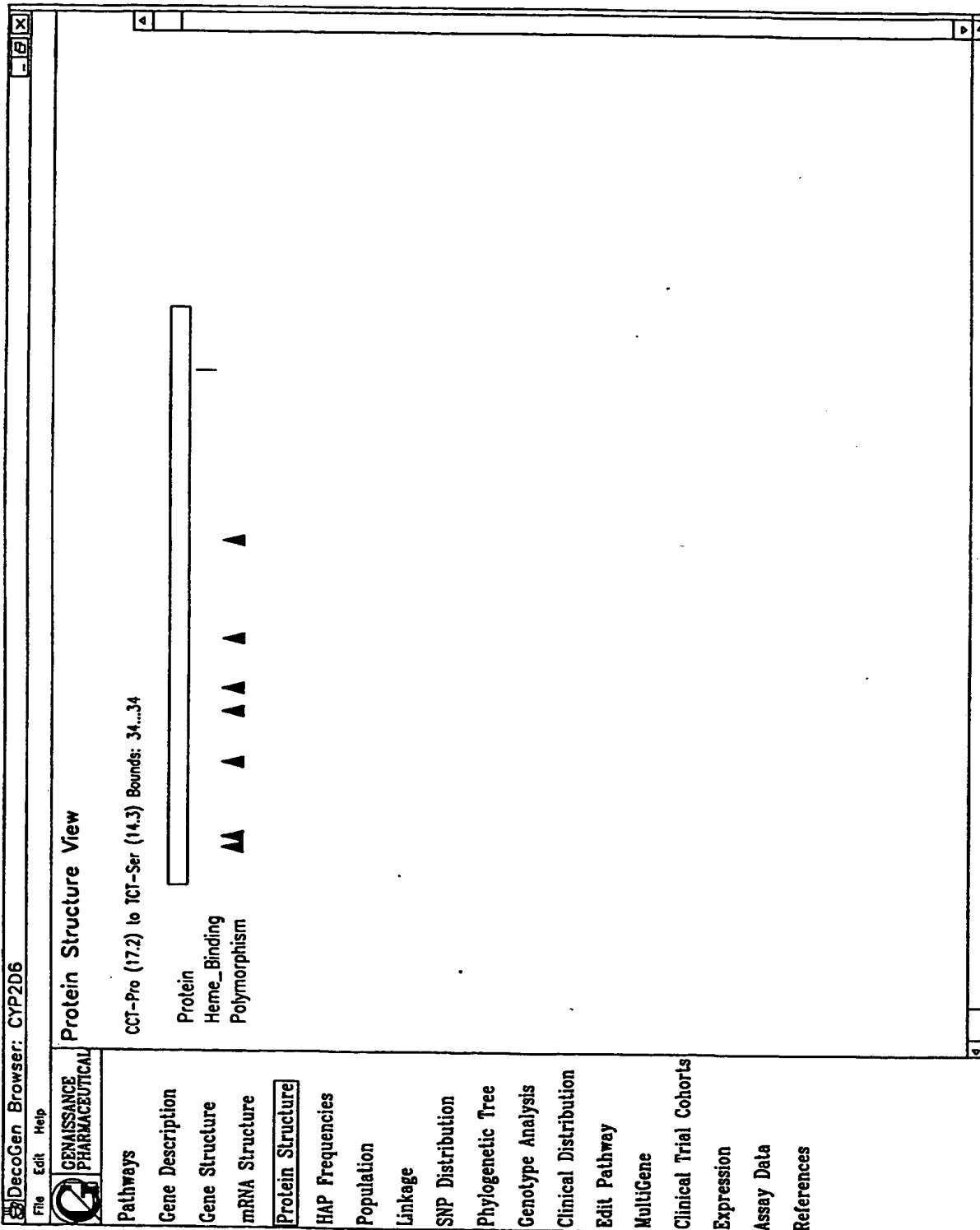
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6. FIG.



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FIG. 7

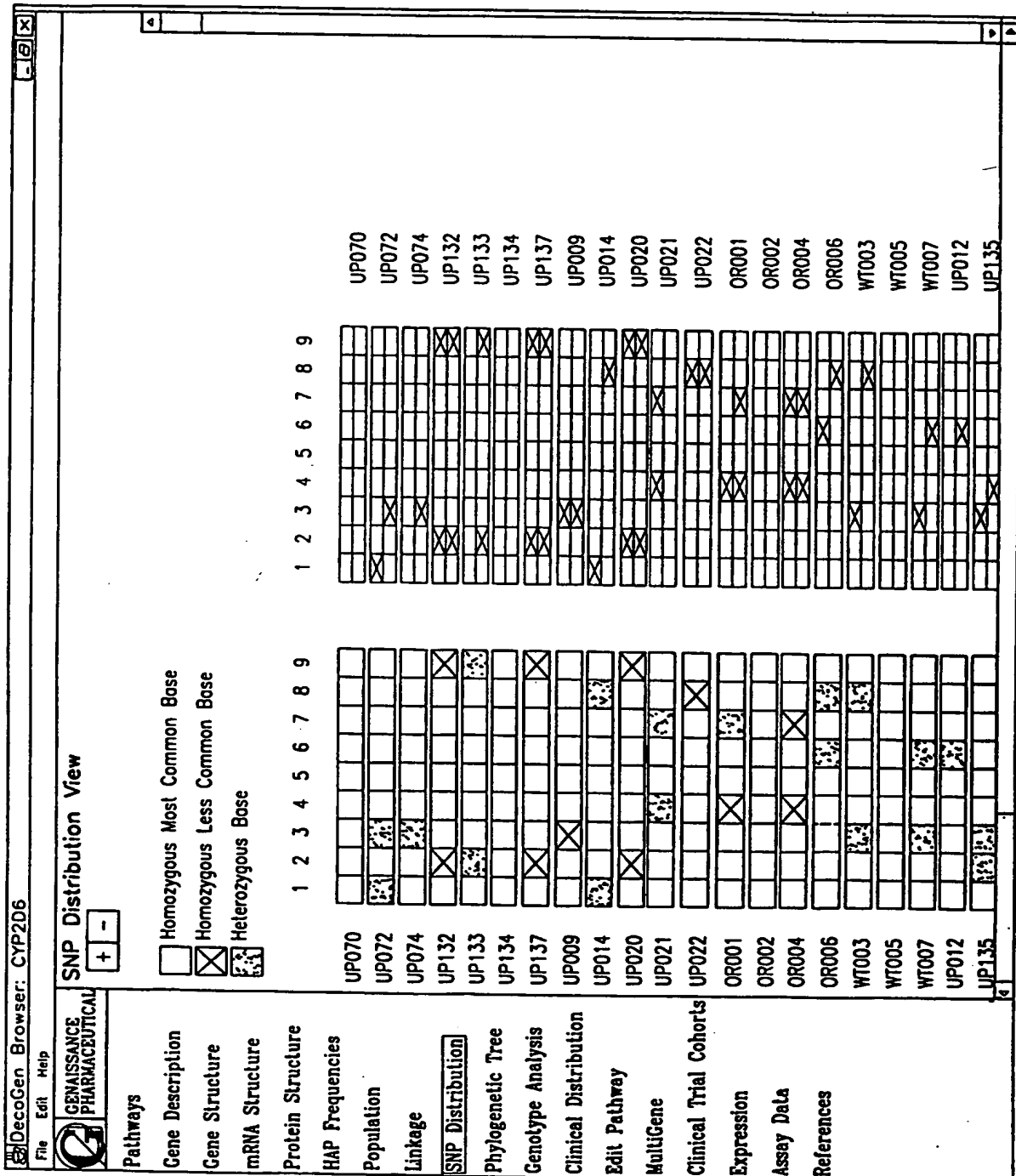


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FIG. 8

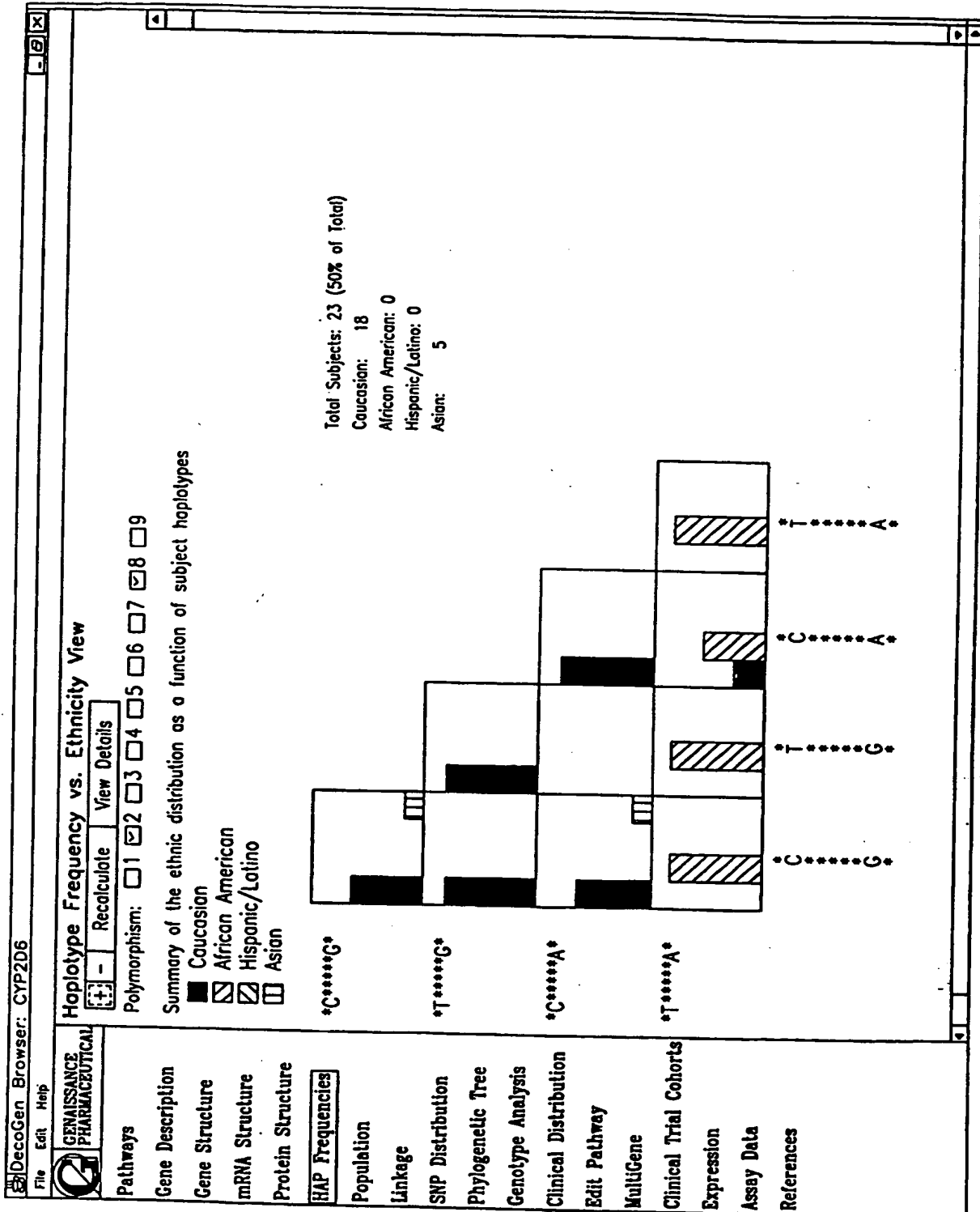
DecoGen Browser: CYP2D6									
File Edit Help									
GENAissance PHARMACEUTICAL									
Population View									
Pathways	PID	Ethnicity	Age	Gender	HAP 1	HAP 2	Test		
Gene Description	UP070	CA	99	F	GGCTGGGC	GGCTGGGC	0.1		
Gene Structure	UP072	CA	99	F	GGCTGGGC	GGCTGGGC	0.2		
mRNA Structure	UP074	CA	99	F	GGCTGGGC	GGCTGGGC	0.2		
Protein Structure	UP132	CA	99	M	GTCTGGGT	GTCTGGGT	0.3		
HAP Frequencies	UP133	CA	99	M	GGCTGGGC	GTCTGGGT	0.2		
Population	UP134	CA	99	F	GGCTGGGC	GGCTGGGC	0.1		
Linkage	UP137	CA	99	M	GTCTGGGT	GTCTGGGT	0.1		
SNP Distribution	UP009	CA	99	F	GGCTGGGC	GGCTGGGC	0.1		
Phylogenetic Tree	UP014	CA	99	F	GGCTGGGC	GGCTGGGC	0.3		
Genotype Analysis	UP020	CA	99	F	GTCTGGGT	GTCTGGGT	0.2		
Clinical Distribution	UP021	CA	99	M	GGCTGGGC	GGCTGGGC	0.4		
Edit Pathway	UP022	CA	99	M	GGCTGGGC	GGCTGGGC	0.3		
MultiGene	OR001	AS	99	M	GGCTGGGC	GGCTGGGC	0.2		
Clinical Trial Cohorts	OR002	AS	99	M	GGCTGGGC	GGCTGGGC	0.3		
Expression	OR004	AS	99	F	GGCTGGGC	GGCTGGGC	0.2		
Assay Data	OR006	AS	99	F	GGCTGGGC	GGCTGGGC	0.1		
References	WT003	CA	99	F	GGCTGGGC	GGCTGGGC	0.2		
	WT005	CA	99	M	GGCTGGGC	GGCTGGGC	0.2		
	WT007	CA	99	M	GGCTGGGC	GGCTGGGC	0.4		
	UP012	CA	99	F	GGCTGGGC	GGCTGGGC	0.1		
	UP135	CA	99	M	GGCTGGGC	GGCTGGGC	0.2		

FIG. 9



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FIG. 10



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FIG. 11

DecoGen Browser: CYP2D6

File Edit Help

GEMSAIANCE PHARMACEUTICAL

Haplotype Frequency vs. Ethnicity View

+ - Recalculate View Summary

Polymorphism: ☐ 1 ☒ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☒ 8 ☐ 9

Details of the ethnic distribution as a function of subject haplotypes

3 Columns are given for each Ethnogeographic group:
Total number sampled with HAP pair
Fraction of the ethnogeographic group with that HAP pair
Fraction expected under Hardy-Weinberg equilibrium for that HAP pair

HAP 1	HAP 2	N	%Pop.	Caucasian	African American	Hispanic/Latino	As
*C*****G*	*C*****G*	23	50%	18.56.3% 37.9%	0 0.0% 0.6%	0 0.0% 0.0%	5
*T*****G*	*C*****G*	2	4%	2 6.3% 18.9%	0 0.0% 2.4%	0 0.0% 0.0%	0
*T*****G*	*T*****G*	4	8%	4 12.5% 2.4%	0 0.0% 2.4%	0 0.0% 0.0%	0
*C*****A*	*C*****G*	5	10%	4 12.5% 25.2%	0 0.0% 2.4%	0 0.0% 0.0%	1
*C*****A*	*C*****A*	3	6%	3 9.4% 4.2%	0 0.0% 2.4%	0 0.0% 0.0%	0
*T*****A*	*C*****G*	1	2%	0 0.0% 3.2%	1 12.5% 9.5%	0 0.0% 0.0%	0
*T*****A*	*T*****G*	2	4%	0 0.0% 0.8%	2 25.0% 18.9%	0 0.0% 0.0%	0
*T*****A*	*C*****A*	3	6%	1 3.1% 1.1%	2 25.0% 18.9%	0 0.0% 0.0%	0
*T*****A*	*T*****A*	3	6%	0 0.0% 0.1%	3 37.5% 37.9%	0 0.0% 0.0%	0

Pathways

Gene Description

Gene Structure

mRNA Structure

Protein Structure

HAP Frequencies

Population

Linkage

SNP Distribution

Phylogenetic Tree

Genotype Analysis

Clinical Distribution

Edit Pathway

MultiGene

Clinical Trial Cohorts

Expression

Assay Data

References

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FIG. 12

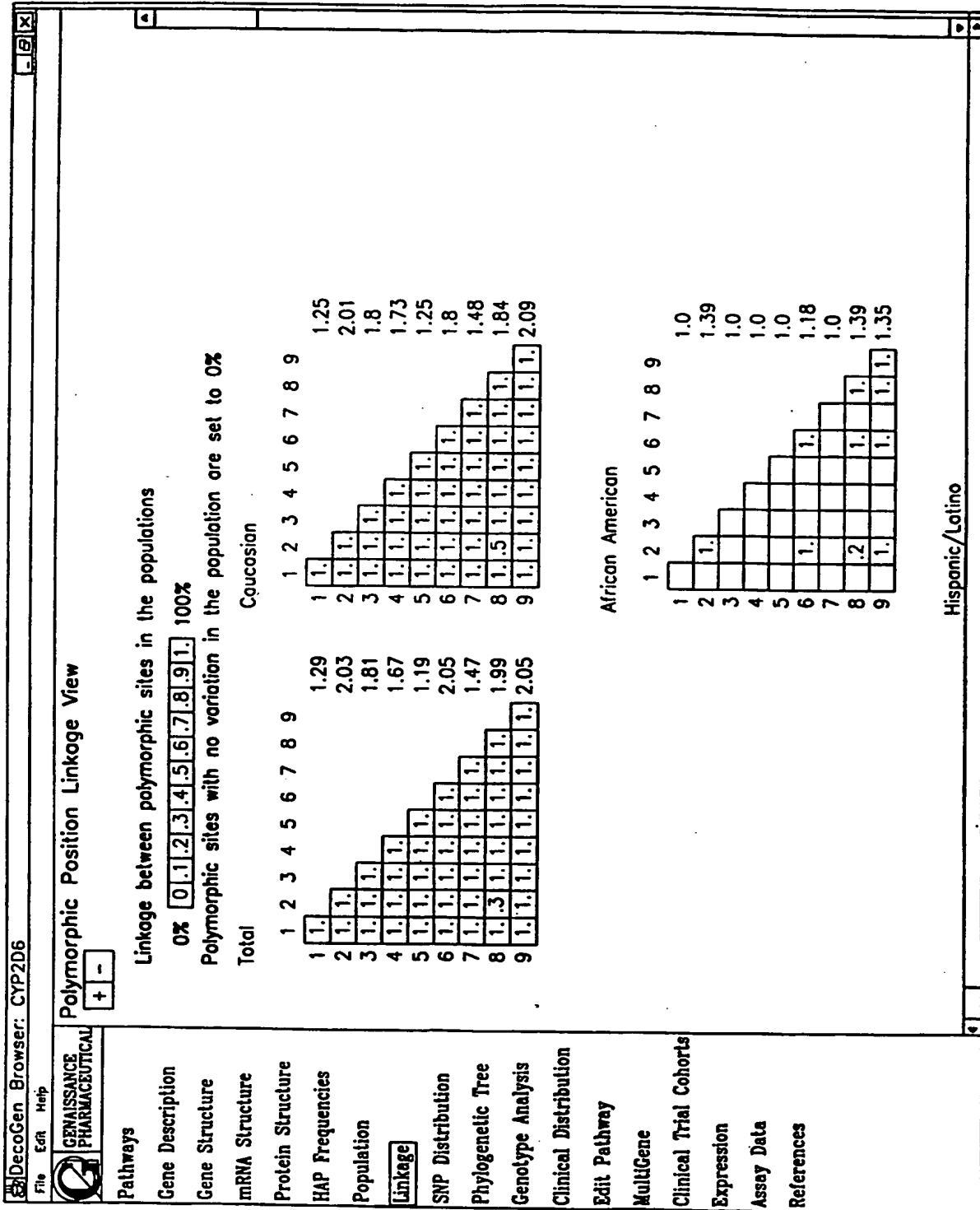
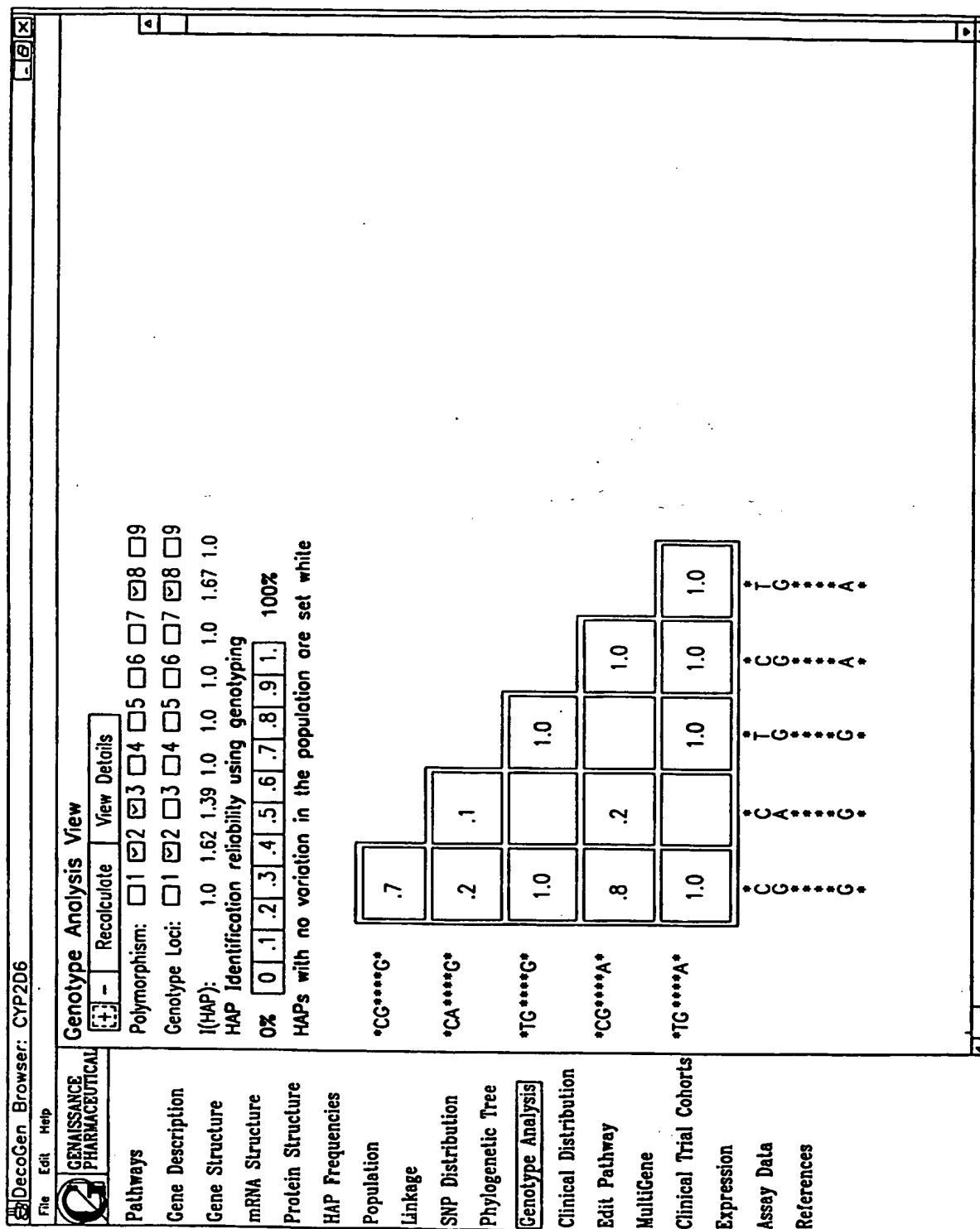


FIG. 13



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FIG. 14

DecoGen Browser: CYP2D6

File Edit Help

GENAISSANCE PHARMACEUTICAL

Pathways

Gene Description

Gene Structure

mRNA Structure

Protein Structure

HAP Frequencies

Population

Linkage

SNP Distribution

Phylogenetic Tree

Genotype Analysis

Clinical Distribution

Edit Pathway

MultiGene

Clinical Trial Cohorts

Expression

Assay Data

References

Genotype Analysis View

+ - Recalculate View Optimized


Polymorphism: ☐ 1 ☒ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☒ 8 ☐ 9

Genotype Loci: ☐ 1 ☒ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☒ 8 ☐ 9

(HAP): 1.0 1.56 1.0 1.0 1.0 1.0 1.0 1.0 1.6 1.0

HAP 1	HAP 2	N	%Pop.	Positive
*C*****G*	*C*****G*	23	50%	100%
*T*****G*	*C*****G*	2	4%	100%
*T*****G*	*T*****G*	4	8%	100%
*C*****A*	*C*****G*	5	10%	100%
*C*****A*	*C*****A*	3	6%	100%
*T*****A*	*C*****G*	1	2%	100%
*T*****A*	*T*****G*	2	4%	100%
*T*****A*	*C*****A*	3	6%	100%
*T*****A*	*T*****A*	3	6%	100%

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DecoGen Browser: CYP2D6

File

Edit

Help



GENAISSANCE

PHARMACEUTICAL

Genotype Analysis View

+

-

Recalculate

View Optimized

Polymorphism:

☐ 1
 ☒ 2
 ☐ 3
 ☐ 4
 ☐ 5
 ☐ 6
 ☐ 7
 ☒ 8
 ☐ 9

I(HAP):

1.0

1.56

1.0

1.0

1.0

1.0

1.0

1.6

1.0

HAP 1	HAP 2	Positive	Mask
*C*****G*	*C*****G*	100%	<input type="checkbox"/>
*T*****G*	*C*****G*	100%	<input type="checkbox"/>
*T*****G*	*T*****G*	100%	<input type="checkbox"/>
*C*****A*	*C*****G*	100%	<input type="checkbox"/>
*C*****A*	*C*****A*	100%	<input type="checkbox"/>
*T*****A*	*C*****G*	100%	<input type="checkbox"/>
*T*****A*	*T*****G*	100%	<input type="checkbox"/>
*T*****A*	*C*****A*	100%	<input type="checkbox"/>
*T*****A*	*T*****A*	100%	<input type="checkbox"/>

Pathways

Gene Description

Gene Structure

mRNA Structure

Protein Structure

HAP Frequencies

Population

Linkage

SNP Distribution

Phylogenetic Tree

Genotype Analysis

Clinical Distribution

Edit Pathway

MultiGene

Clinical Trial Cohorts

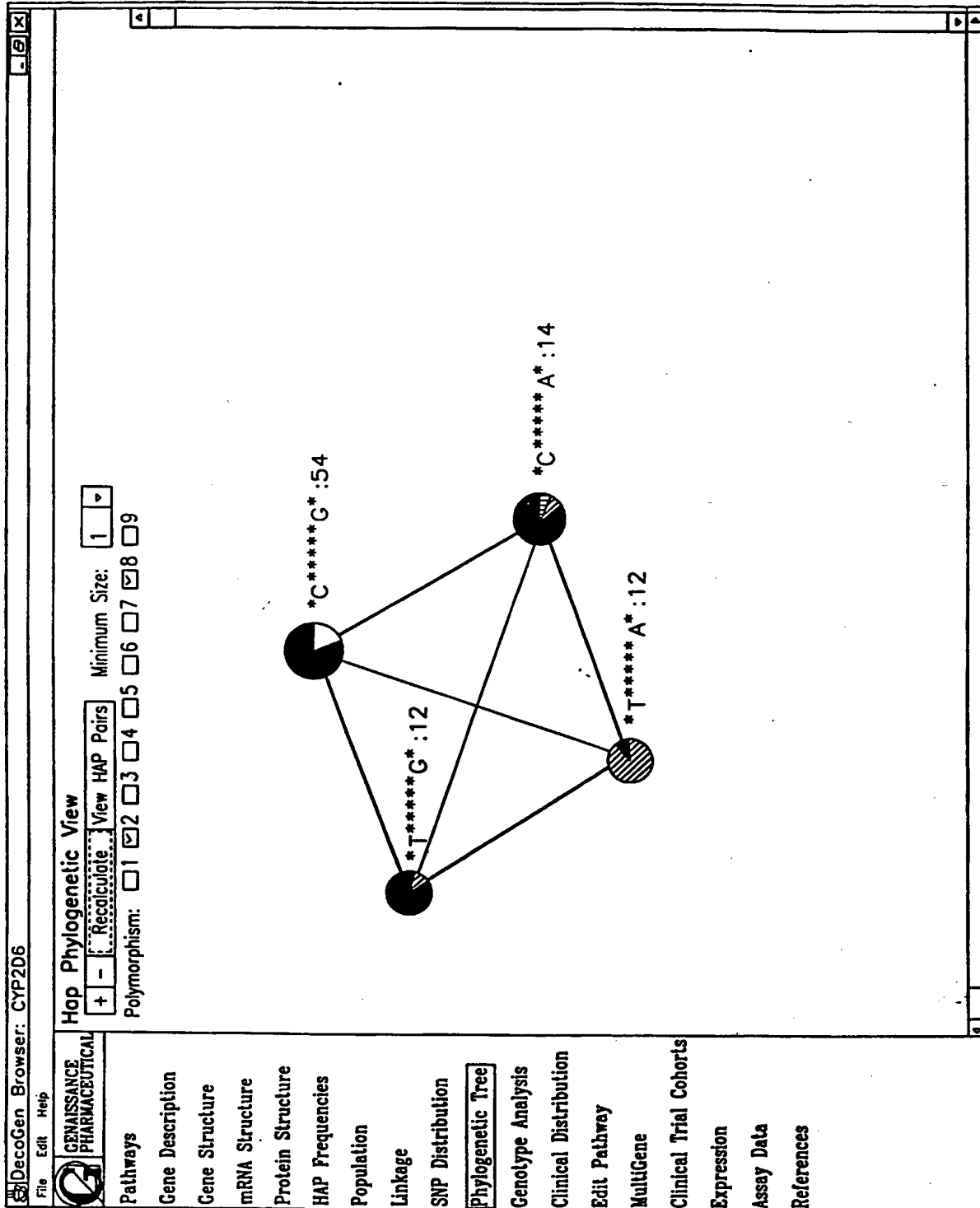
Expression

Assay Data

References

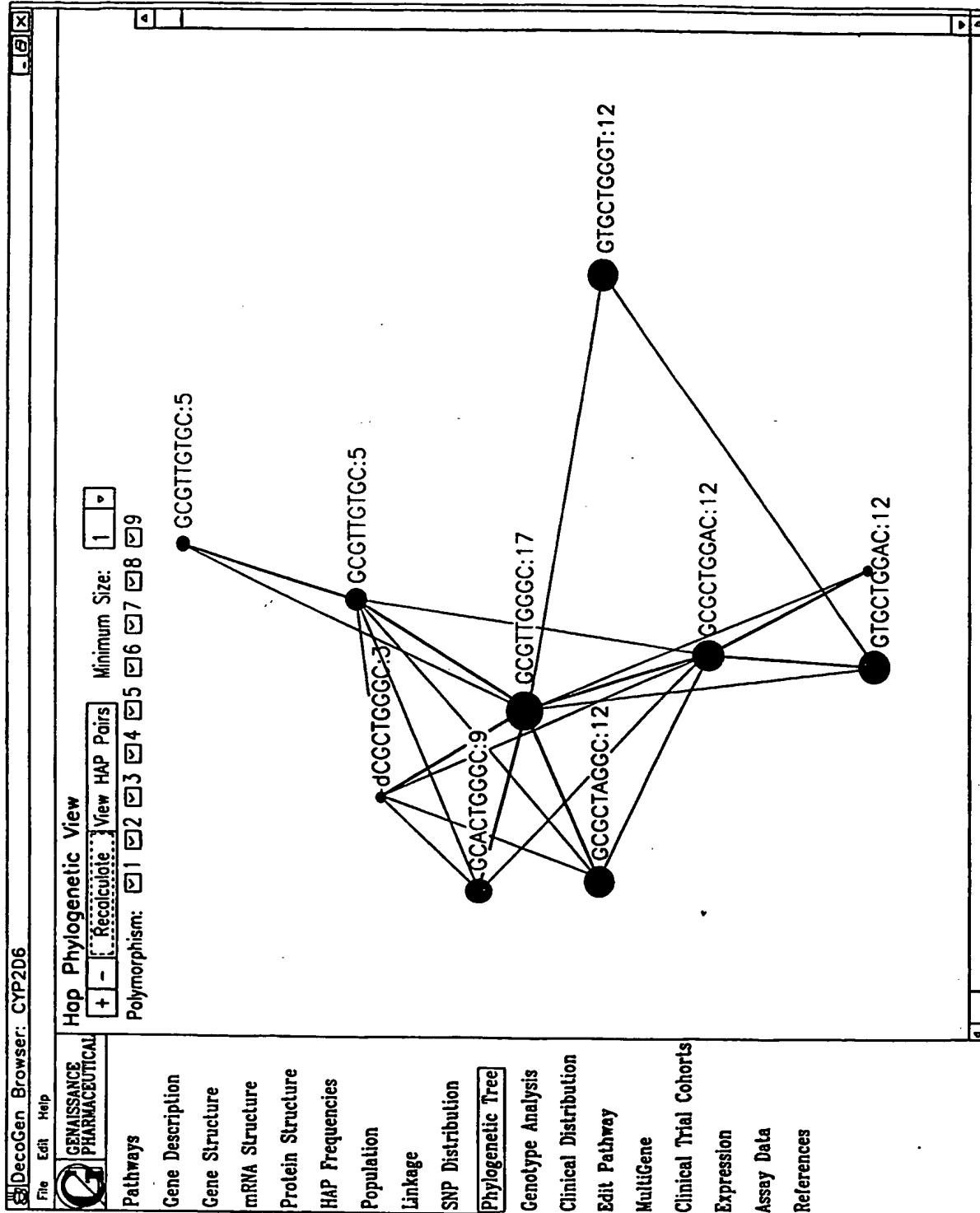
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FIG. 16



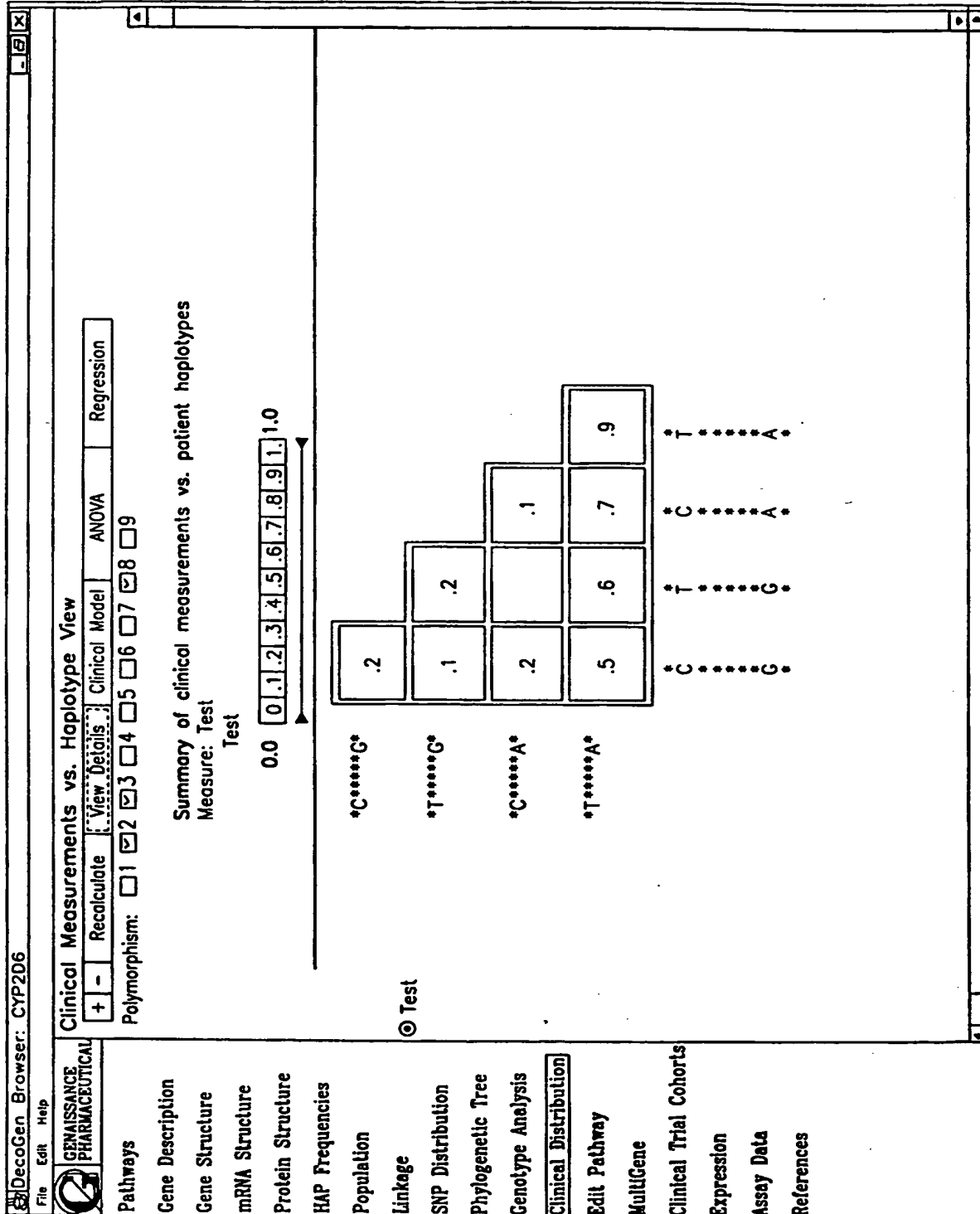
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FIG. 17

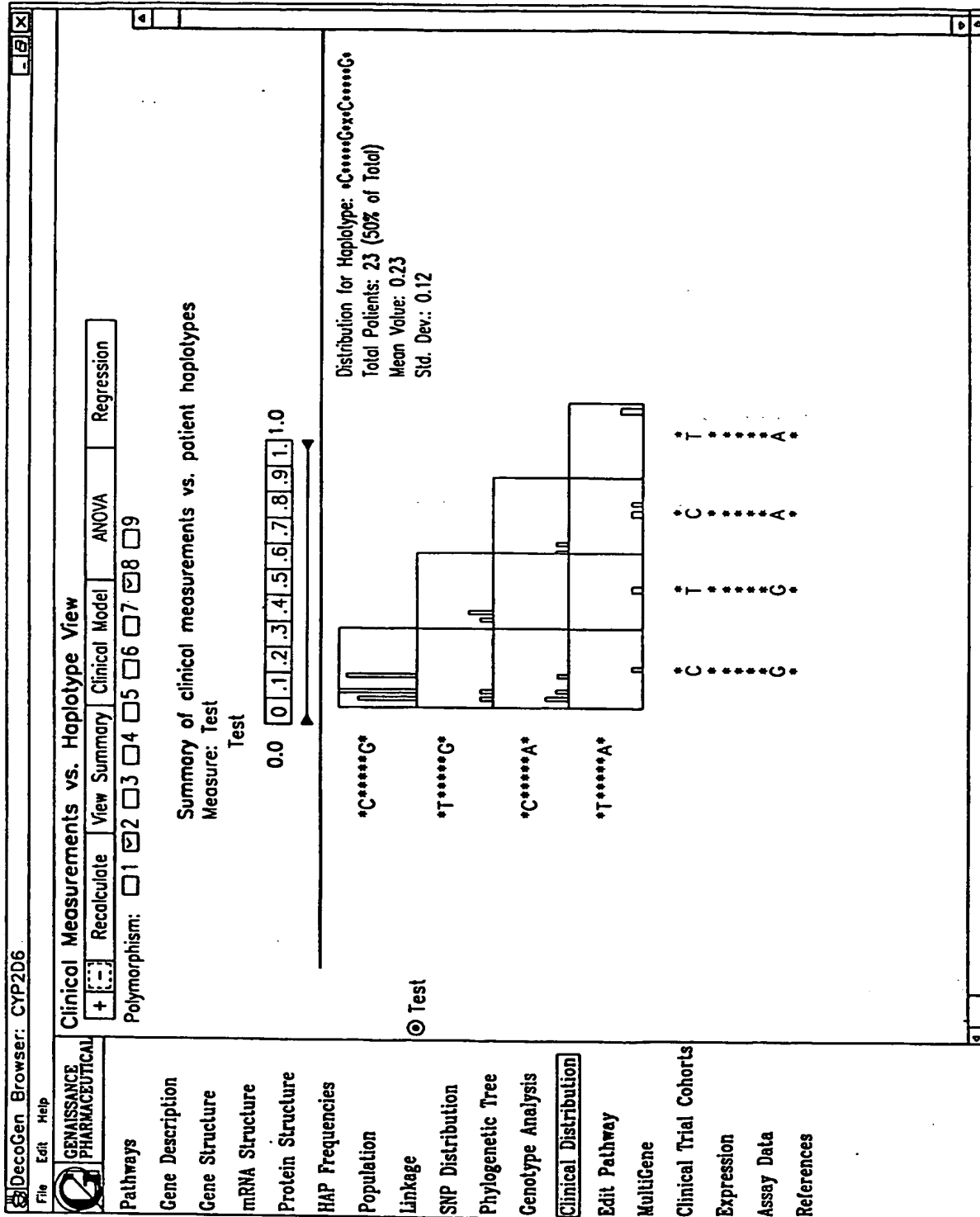


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FIG. 18



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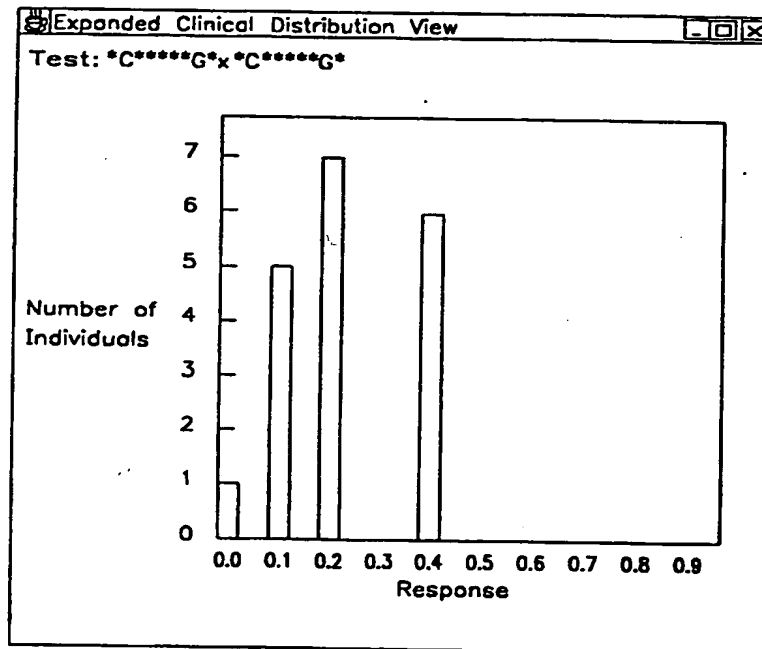
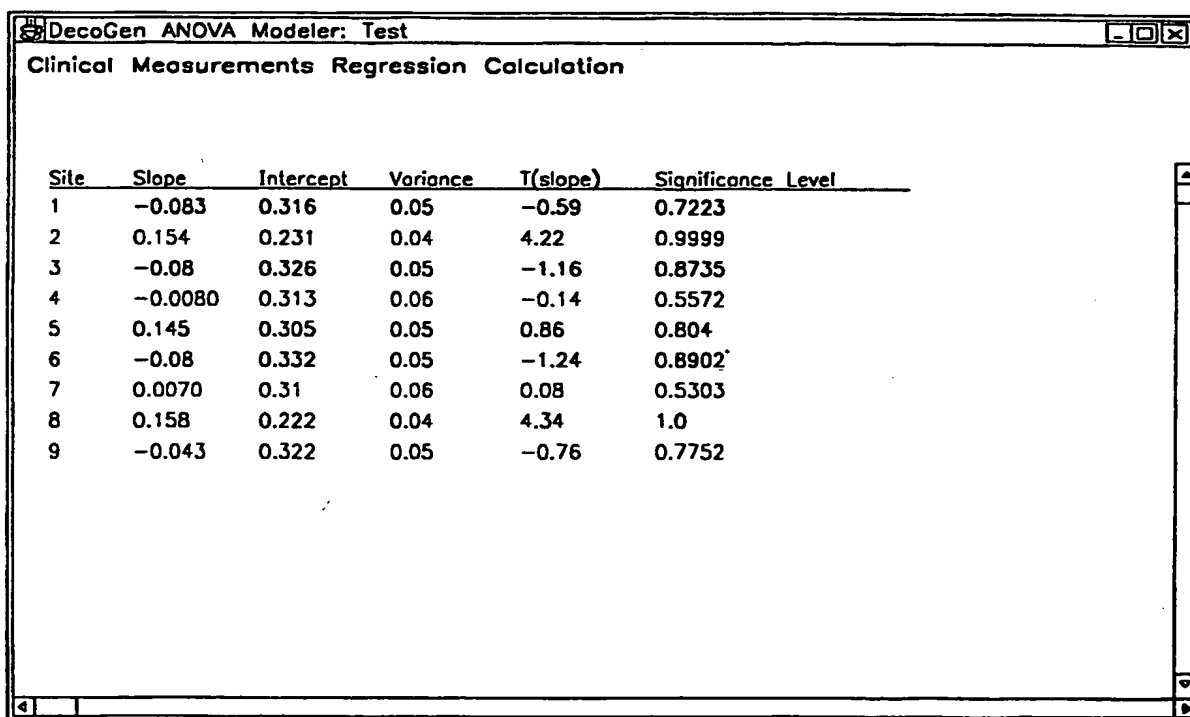


FIG. 20

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DecoGen ANOVA Modeler: Test

Clinical Measurements Regression Calculation

Site	Slope	Intercept	Variance	T(slope)	Significance Level
1	-0.083	0.316	0.05	-0.59	0.7223
2	0.154	0.231	0.04	4.22	0.9999
3	-0.08	0.326	0.05	-1.16	0.8735
4	-0.0080	0.313	0.06	-0.14	0.5572
5	0.145	0.305	0.05	0.86	0.804
6	-0.08	0.332	0.05	-1.24	0.8902
7	0.0070	0.31	0.06	0.08	0.5303
8	0.158	0.222	0.04	4.34	1.0
9	-0.043	0.322	0.05	-0.76	0.7752

FIG. 21

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FIG. 22

DecoGen Browser: CYP2D6

File Edit Help

GENAISSANCE PHARMACEUTICAL

Pathways

Gene Description

Gene Structure

mRNA Structure

Protein Structure

HAP Frequencies

Population

Linkage

SNP Distribution

Phylogenetic Tree

Genotype Analysis

Clinical Distribution

Edit Pathway

MultiGene

Clinical Trial Cohorts

Expression

Assay Data

References

Clinical Measurements vs. Haplotype View

+ - Recalculate View Distribution Clinical Model ANOVA Regression

Polymorphism: ☐ 1 ☒ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☒ 8 ☐ 9

Summary of clinical measurements vs. patient haplotypes

Measure: Test

0.0 0 .1 .2 .3 .4 .5 .6 .7 .8 .9 1.0

Test

HAP 1	Hap 2	N	%Pop.	Mean	Stddev	X**2	Q(X**2 K-3)
*C****G*	*C****G*	23	50%	0.24	0.12	9.17	0.0 (1)
*T****G*	*C****G*	2	4%	0.15	0.07	0.0	1.0 (-3)
*T****G*	*T****G*	4	8%	0.2	0.08	0.0	1.0 (-3)
*C****A*	*C****G*	5	10%	0.22	0.13	0.8	1.0 (-2)
*C****A*	*C****A*	3	6%	0.13	0.15	0.0	1.0 (-3)
*T****A*	*C****G*	1	2%	0.5	0.0	0.0	1.0 (-3)
*T****A*	*T****G*	2	4%	0.55	0.07	0.0	1.0 (-3)
*T****A*	*C****A*	3	6%	.6	0.1	0.0	1.0 (-3)
*T****A*	*T****A*	3	6%	0.93	0.06	0.0	1.0 (-3)

Test

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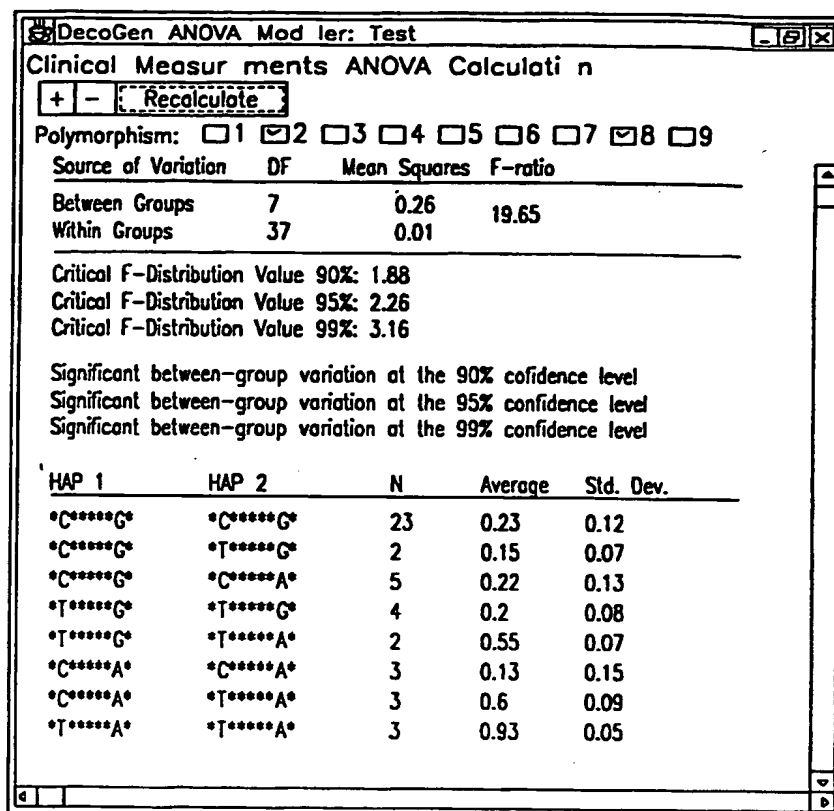


FIG. 23

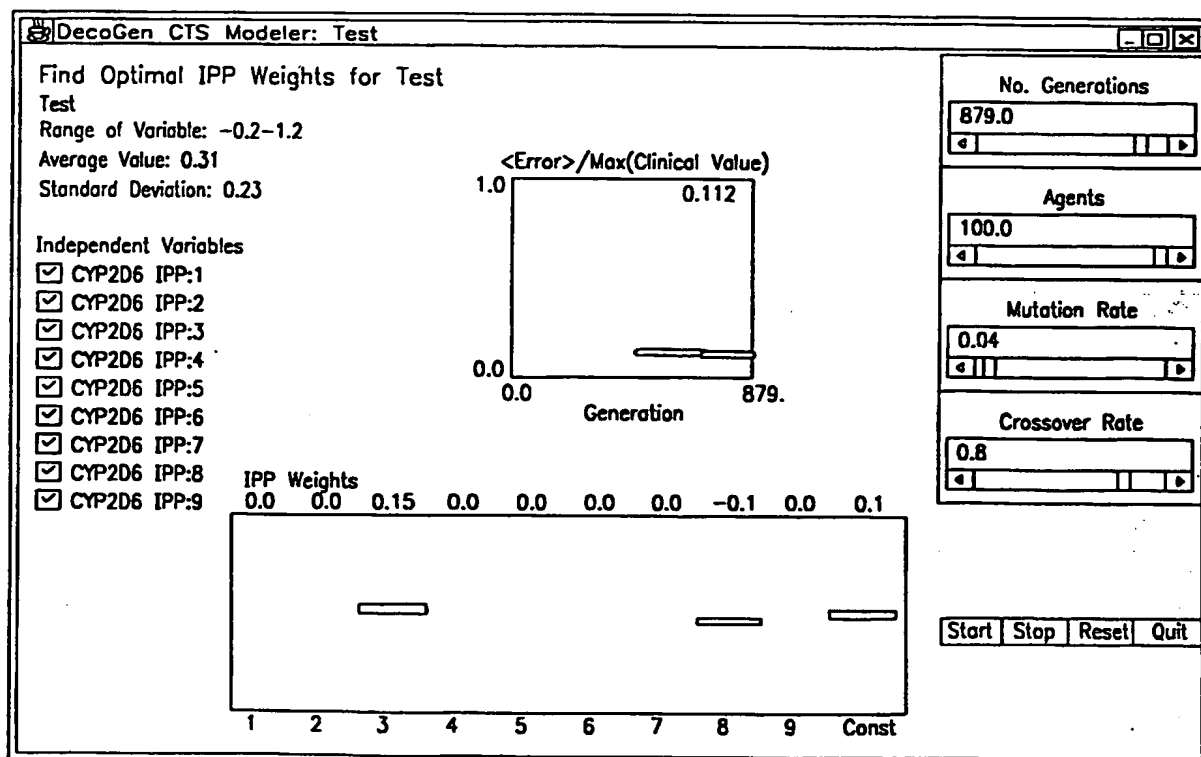


FIG. 24

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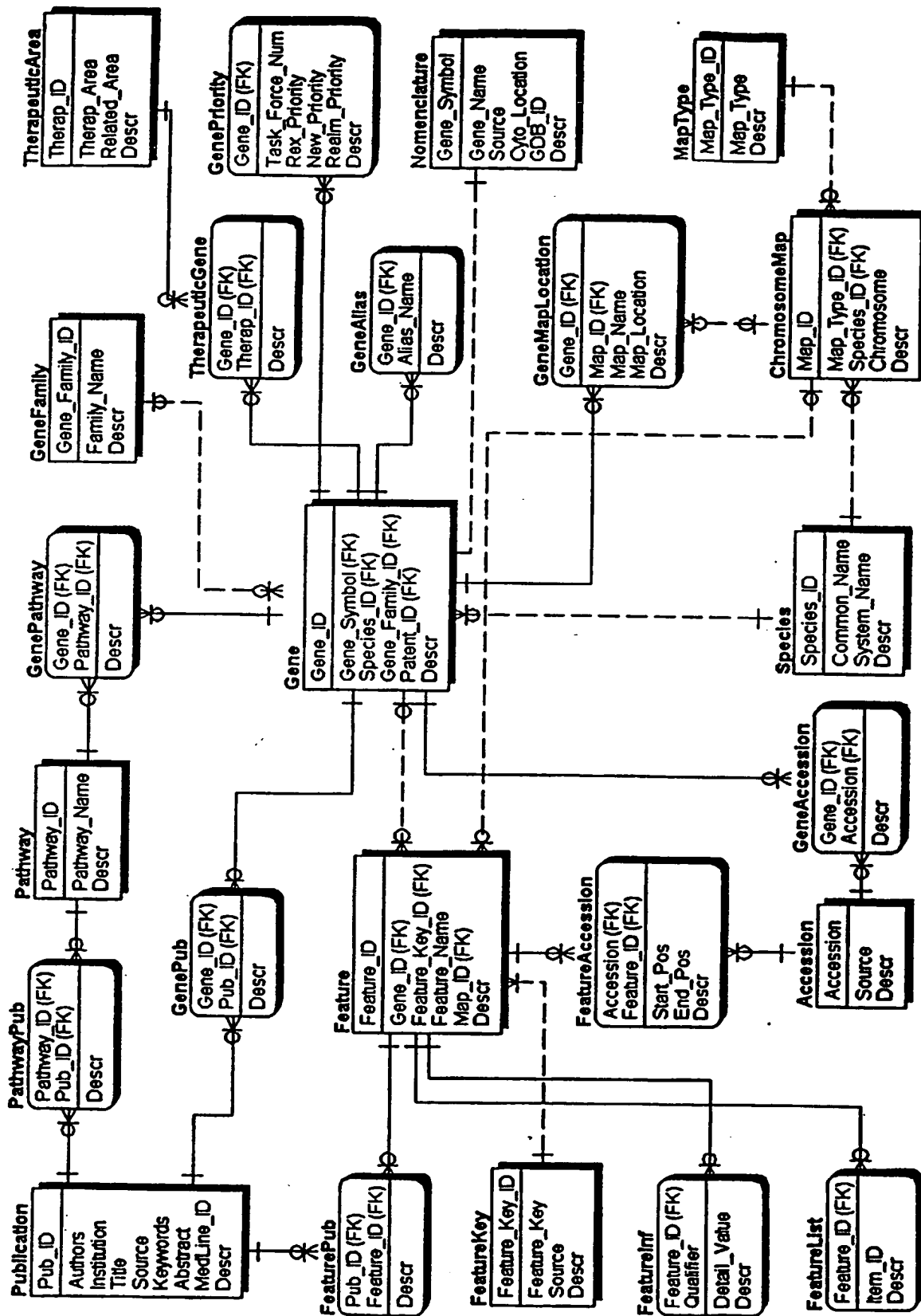
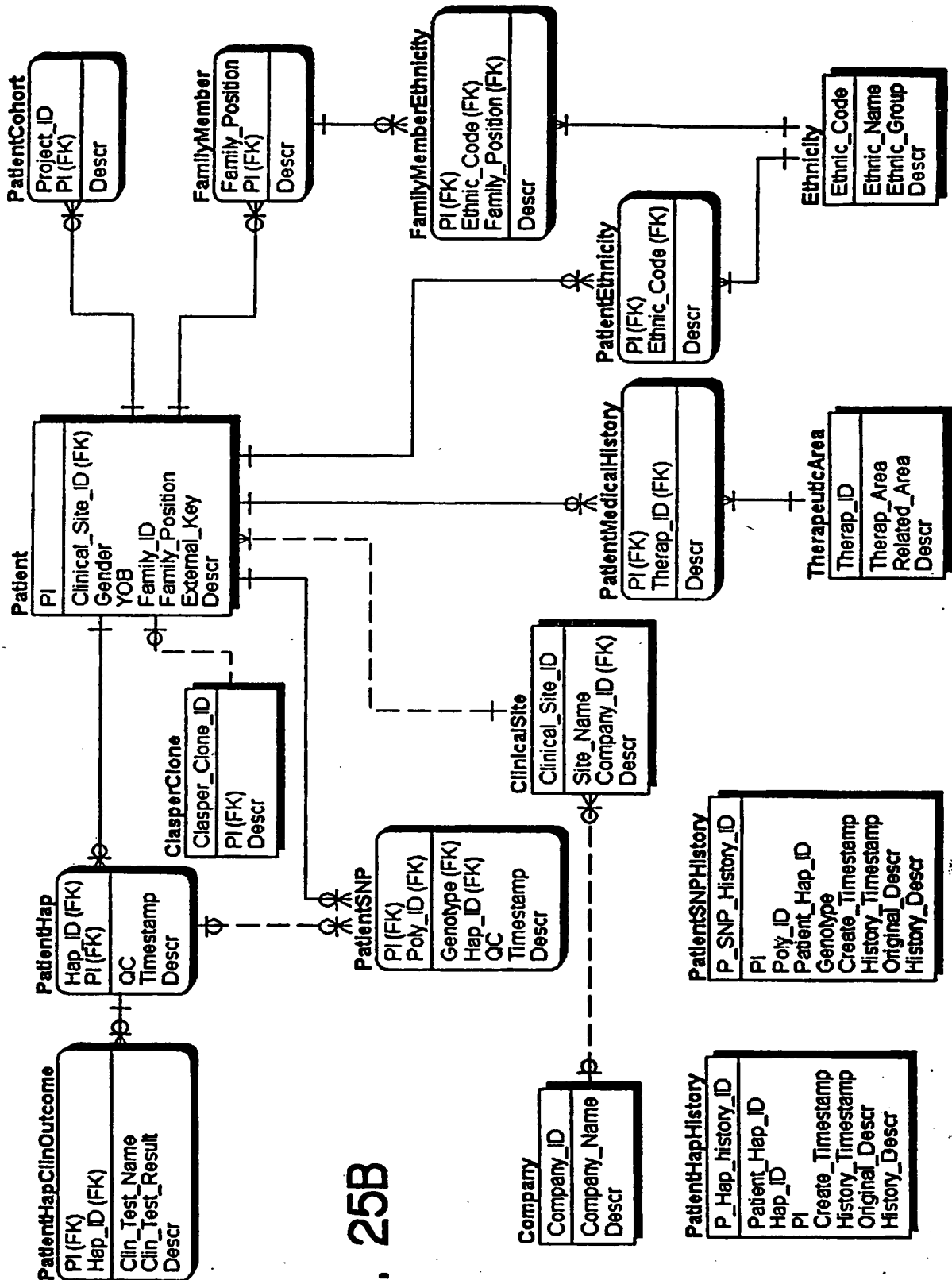


FIG. 25A

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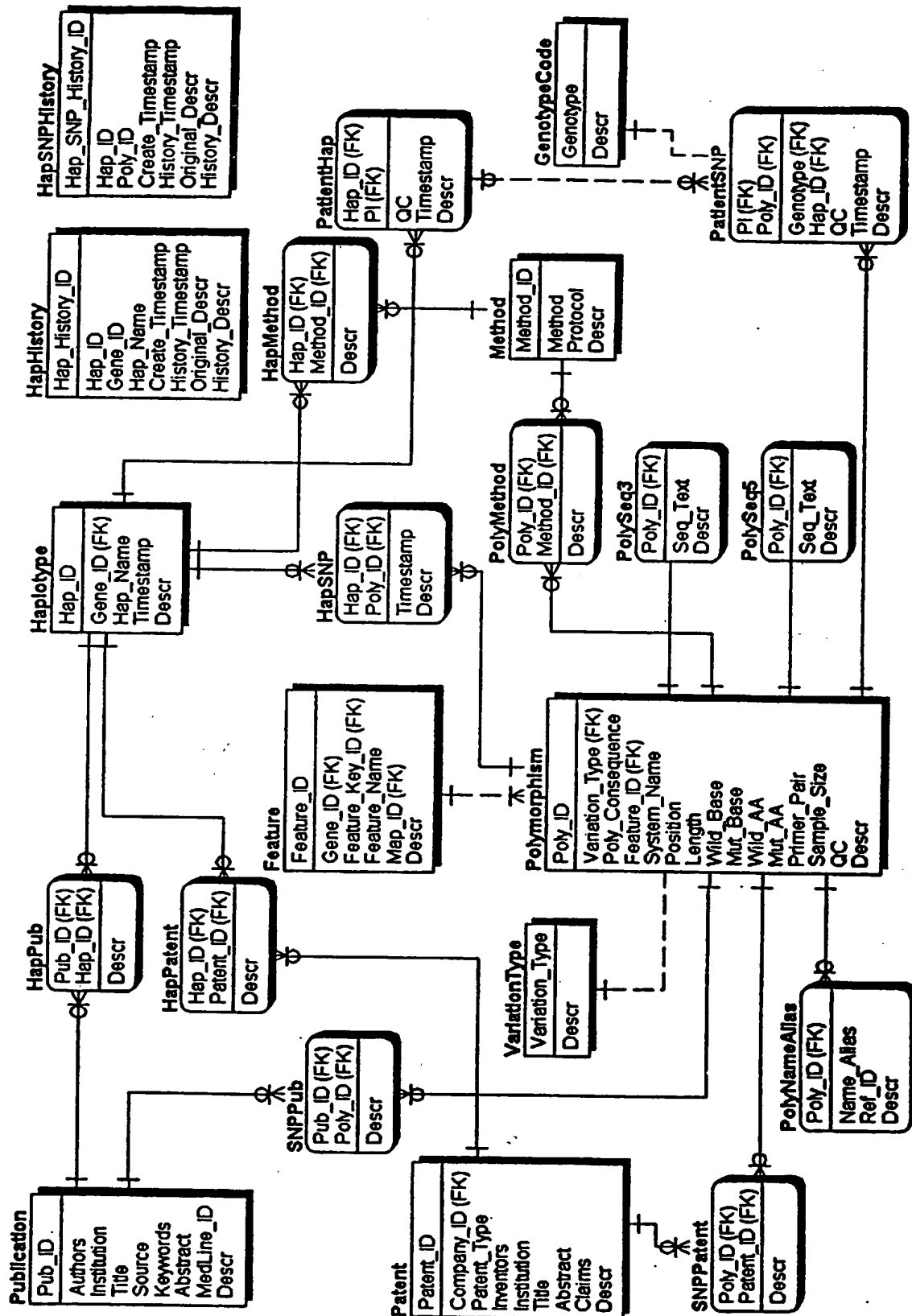


FIG. 25C

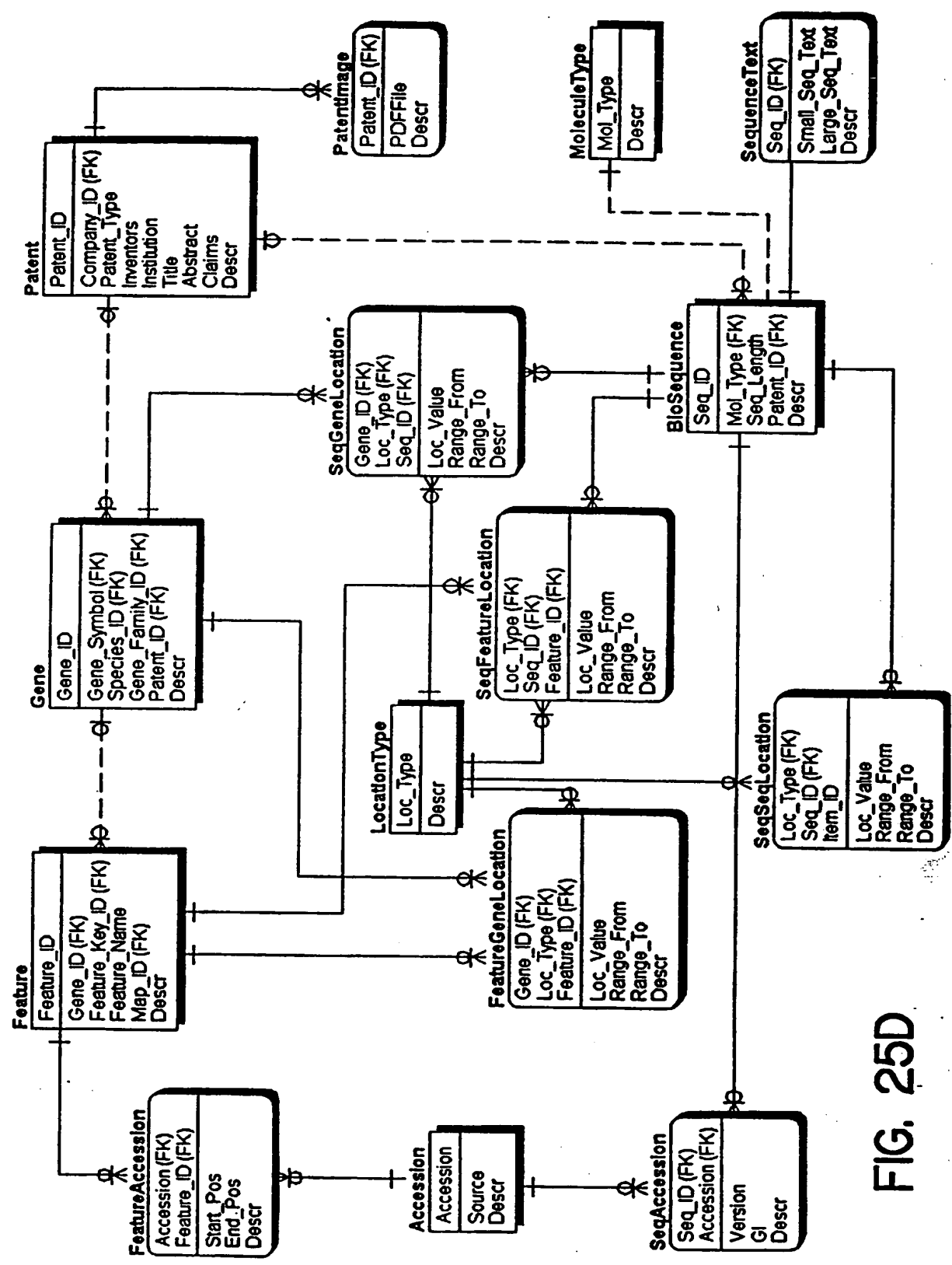


FIG. 25D

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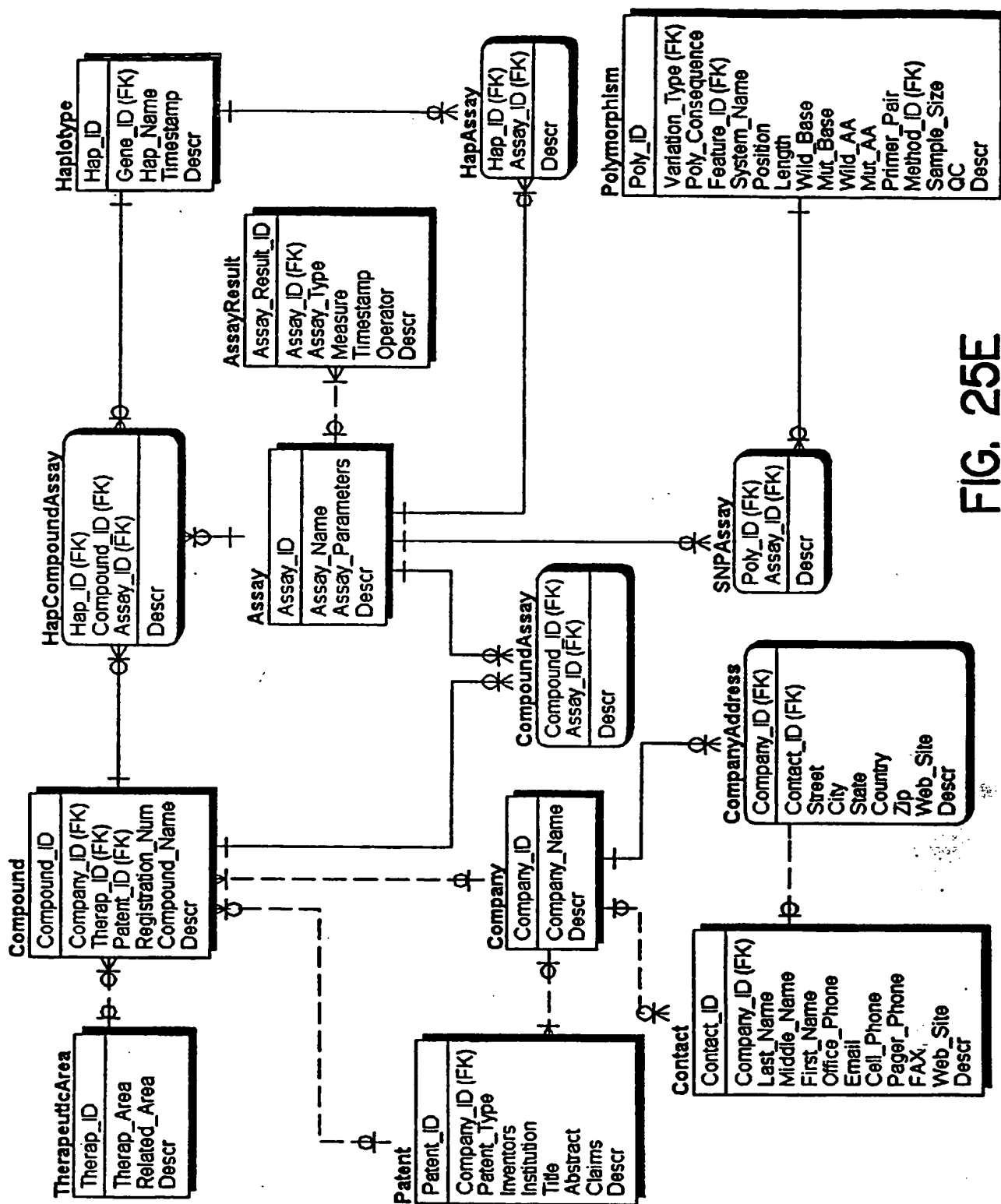


FIG. 25E

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Legend of Figures:

Rectangle Boxes: Tables in the database.



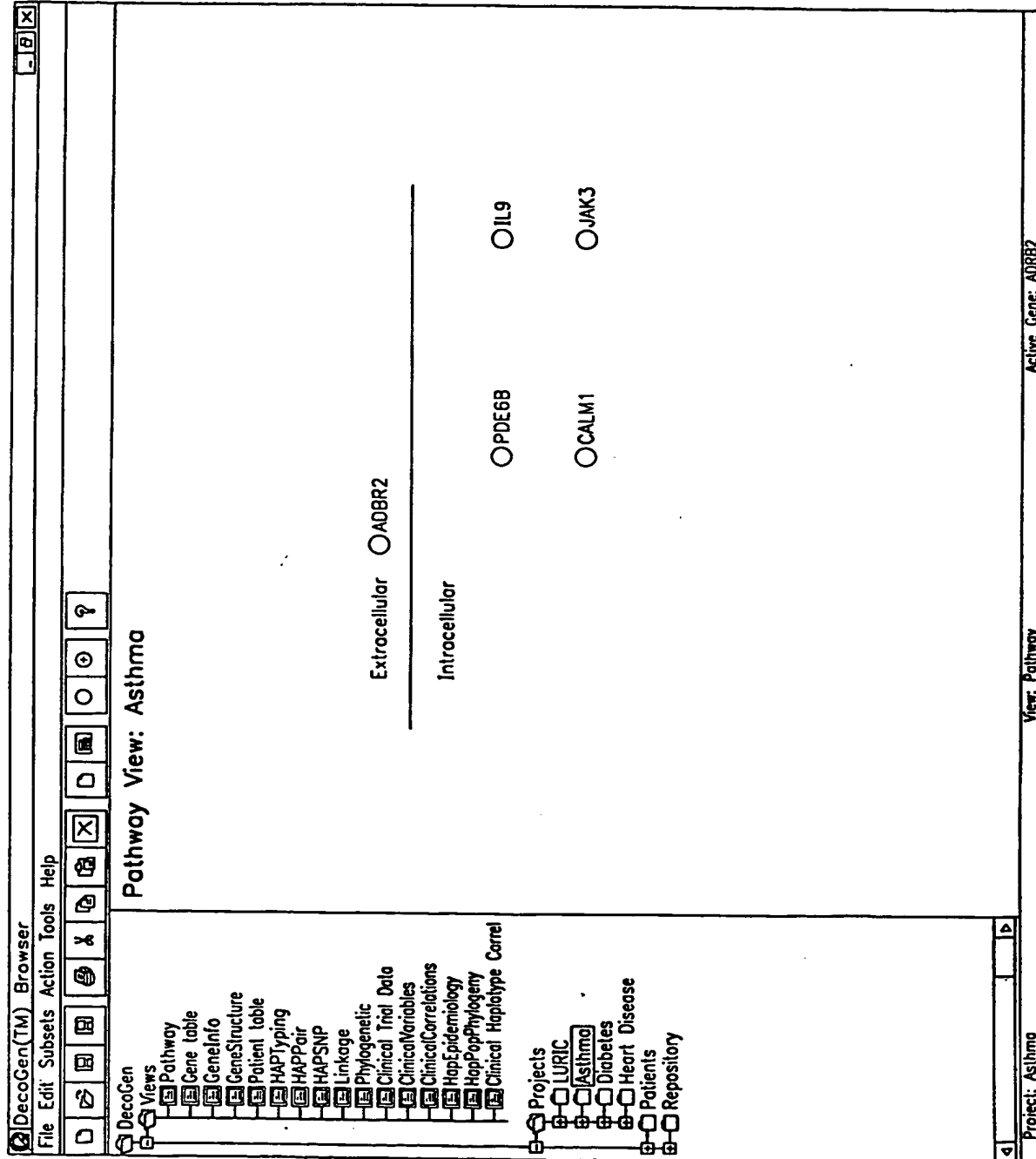
Rounded Boxes: Children tables that depend on their parent tables. This dependency requires that a parent record to be in existence before a child record can be created.

- 2: ————* Identifying parent / child relationship. It depicts the not nullable 1-to-0-or-many relationship.
- 4: ————* Non-identifying parent / child relationship. It represents the nullable 0-or-1-to-many relationship.
- 6: ————* Identifying parent / child relationship. It depicts the not nullable 1-to-1-or-many relationship.
- 8: - - - - * Non-identifying parent / child relationship. It represents the not nullable 1-to-1-or-many relationship.
- 10: |——— Non-identifying parent / child relationship. It represents the nullable 0-or-1-to-many relationship.
- 12: |——— Non-identifying parent / child relationship. It represents the nullable 0-or-1-to-exact-1 relationship.
- 14: |———* Non-identifying parent / child relationship. It represents the not nullable 0-or-1-to-many relationship.

FIG. 25F


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FIG. 26



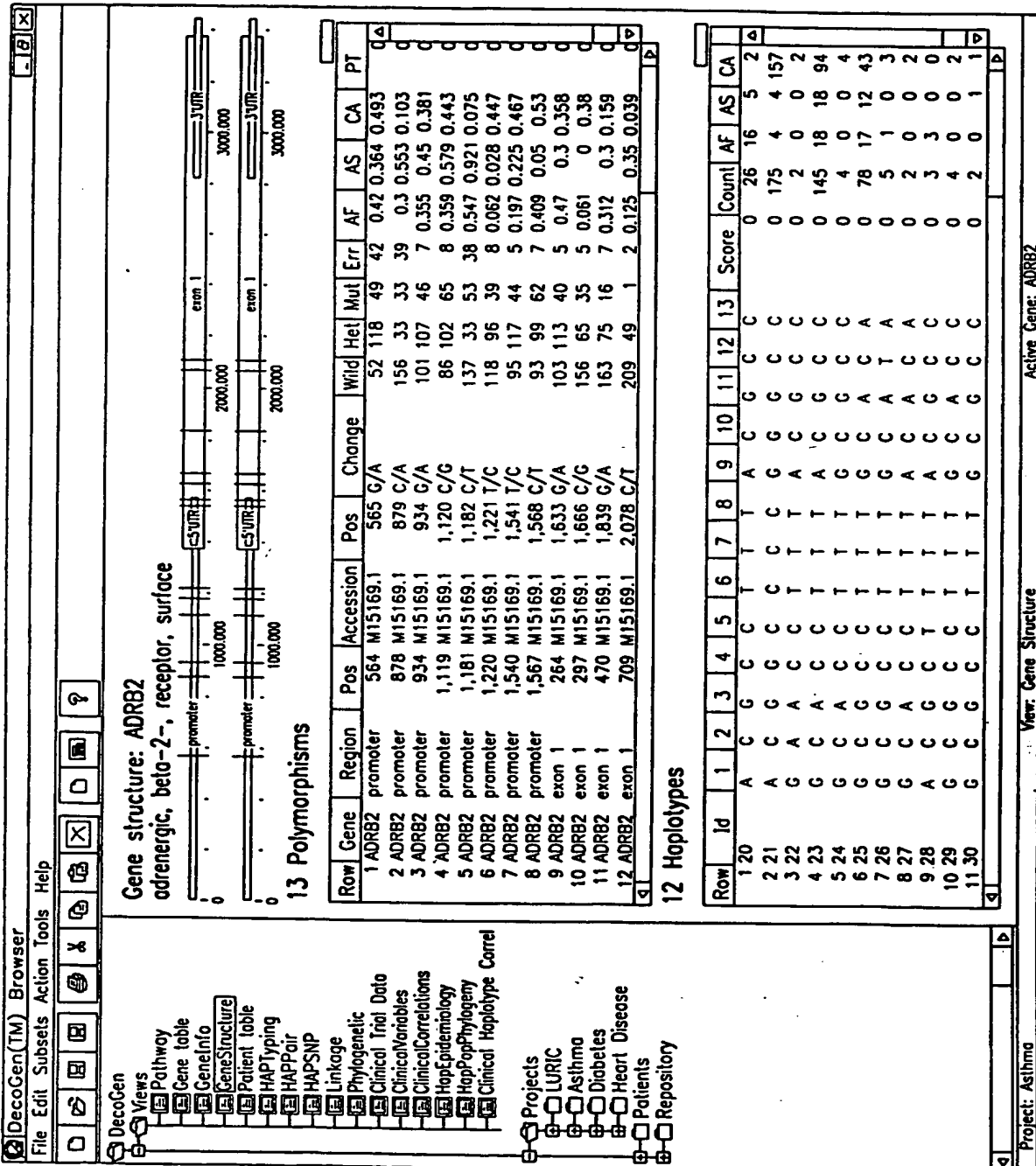
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FIG. 27

DecoGen(TM) Browser																								
File Edit Subsets Action Tools Help																								
																								
<div>DecoGen Views</div> <ul style="list-style-type: none"><input checked="" type="checkbox"/> Pathway<input checked="" type="checkbox"/> Gene table<input checked="" type="checkbox"/> GeneInfo<input checked="" type="checkbox"/> GeneStructure<input checked="" type="checkbox"/> Patient table<input checked="" type="checkbox"/> HAPtyping<input checked="" type="checkbox"/> HAPPair<input checked="" type="checkbox"/> HAPSNP<input checked="" type="checkbox"/> Linkage<input checked="" type="checkbox"/> Phylogenetic<input checked="" type="checkbox"/> Clinical Trial Data<input checked="" type="checkbox"/> ClinicalVariables<input checked="" type="checkbox"/> ClinicalCorrelations<input checked="" type="checkbox"/> HapEpidemiology<input checked="" type="checkbox"/> HapPopPhylogeny<input checked="" type="checkbox"/> Clinical Haplotype Correl<input type="checkbox"/> Projects<input type="checkbox"/> LURIC<input type="checkbox"/> Asthma<input type="checkbox"/> Diabetes<input type="checkbox"/> Heart Disease<input type="checkbox"/> Patients<input type="checkbox"/> Repository		<div>Gene Description View</div> <table border="1"><tr><td>Name</td><td>ADRB2</td></tr><tr><td>Definition</td><td>adrenergic, beta-2-, receptor, surface</td></tr><tr><td>Function</td><td>Function</td></tr><tr><td>Organism</td><td>Human</td></tr><tr><td>Length</td><td>3451</td></tr><tr><td>No. Features</td><td>5</td></tr><tr><td>Population Size</td><td>261</td></tr><tr><td>No. Haplotypes</td><td>12</td></tr><tr><td>No. SNPs</td><td>13</td></tr><tr><td>Nucleotide Polymorphism (Ihelo)</td><td>7.9E-4 +/-3.9E-4</td></tr><tr><td>Nucleotide Diversity (pi)</td><td>4.6E-4 +/-2.8E-4</td></tr></table>	Name	ADRB2	Definition	adrenergic, beta-2-, receptor, surface	Function	Function	Organism	Human	Length	3451	No. Features	5	Population Size	261	No. Haplotypes	12	No. SNPs	13	Nucleotide Polymorphism (Ihelo)	7.9E-4 +/-3.9E-4	Nucleotide Diversity (pi)	4.6E-4 +/-2.8E-4
Name	ADRB2																							
Definition	adrenergic, beta-2-, receptor, surface																							
Function	Function																							
Organism	Human																							
Length	3451																							
No. Features	5																							
Population Size	261																							
No. Haplotypes	12																							
No. SNPs	13																							
Nucleotide Polymorphism (Ihelo)	7.9E-4 +/-3.9E-4																							
Nucleotide Diversity (pi)	4.6E-4 +/-2.8E-4																							
Project: Asthma	View: GeneInfo Active Gene: ADRB2																							

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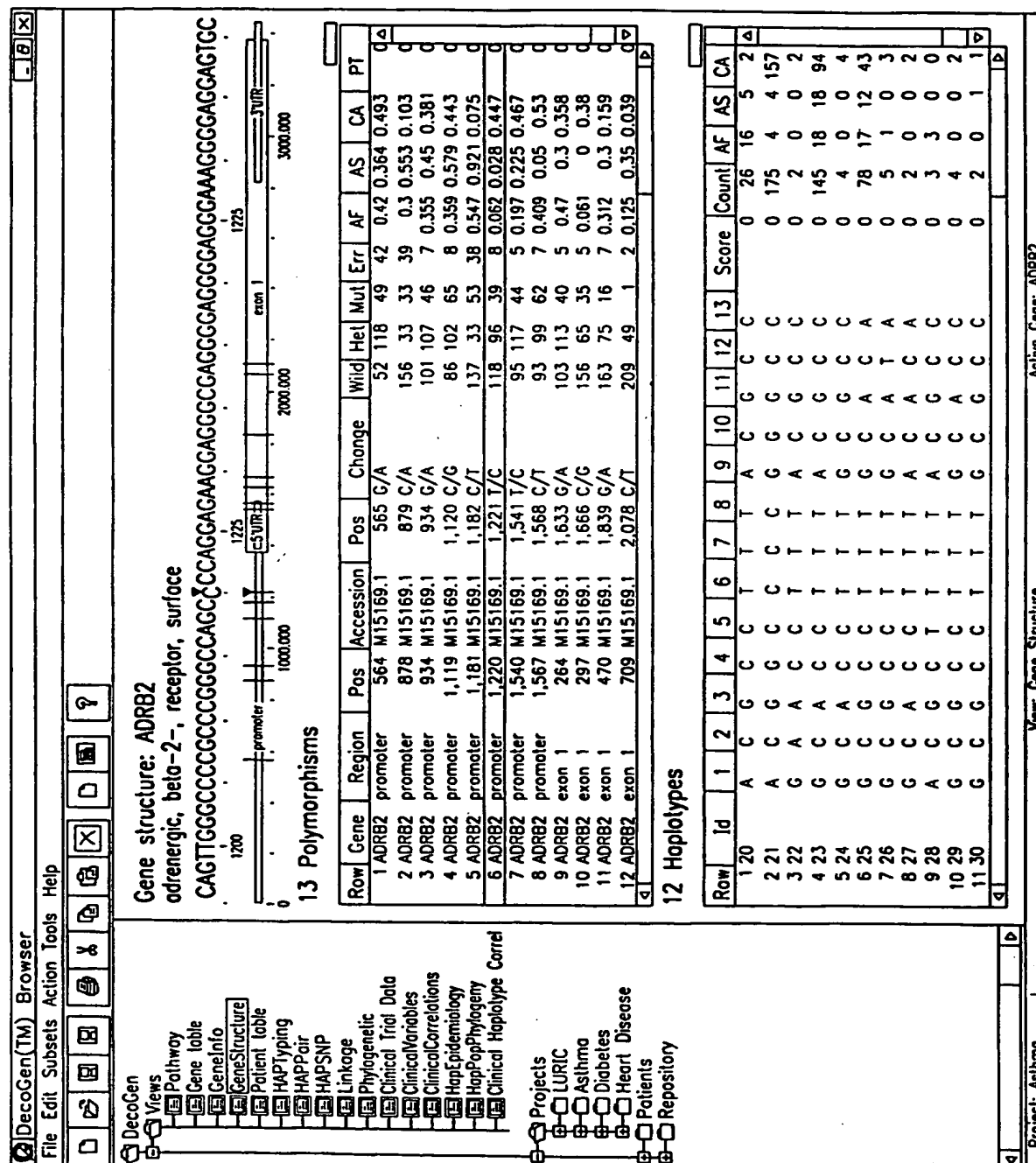
FIG. 28A



SUBSTITUTE SHEET (RULE 26)

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FIG. 28B



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FIG. 29A

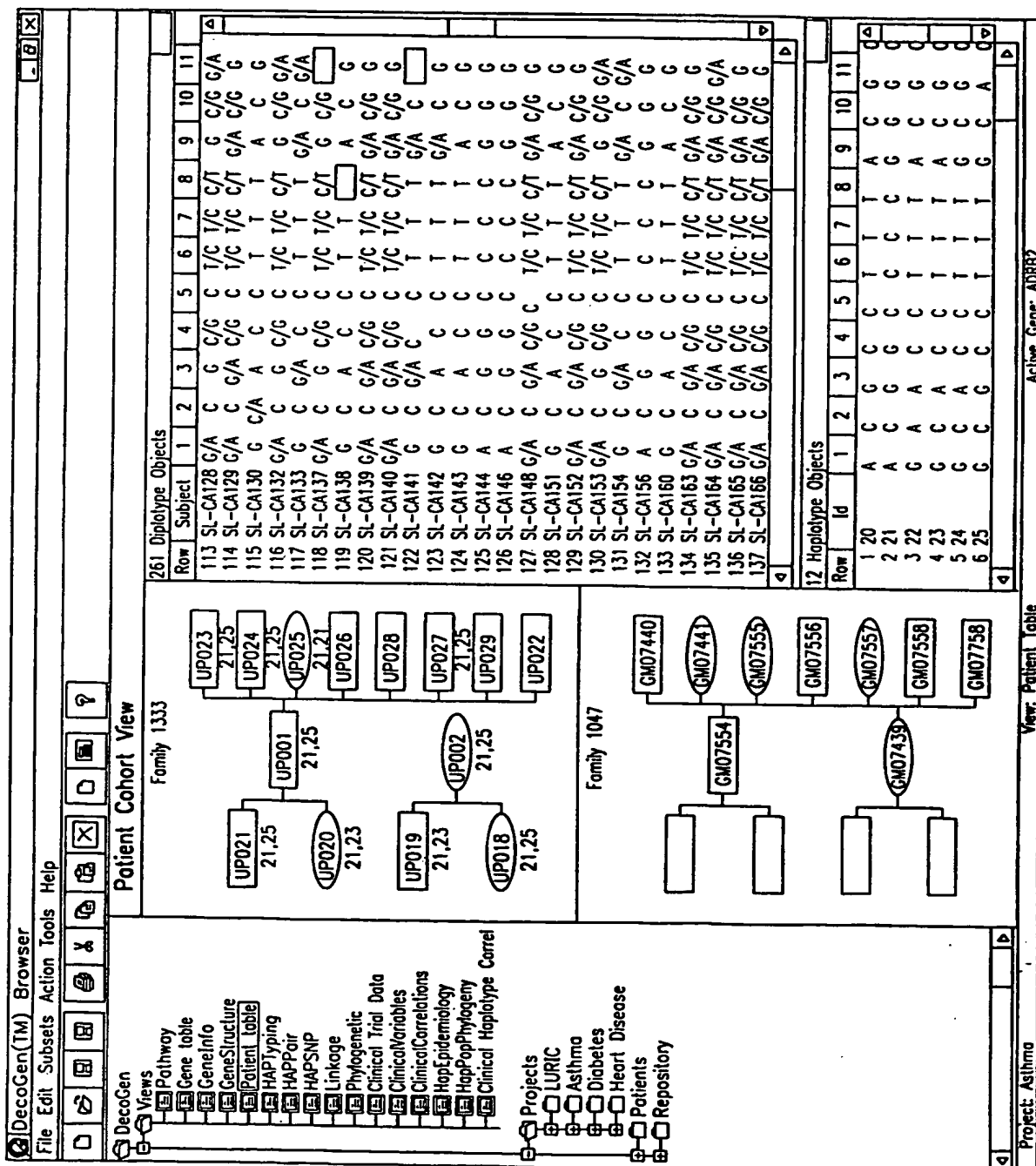


FIG. 29B

<

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FIG. 30

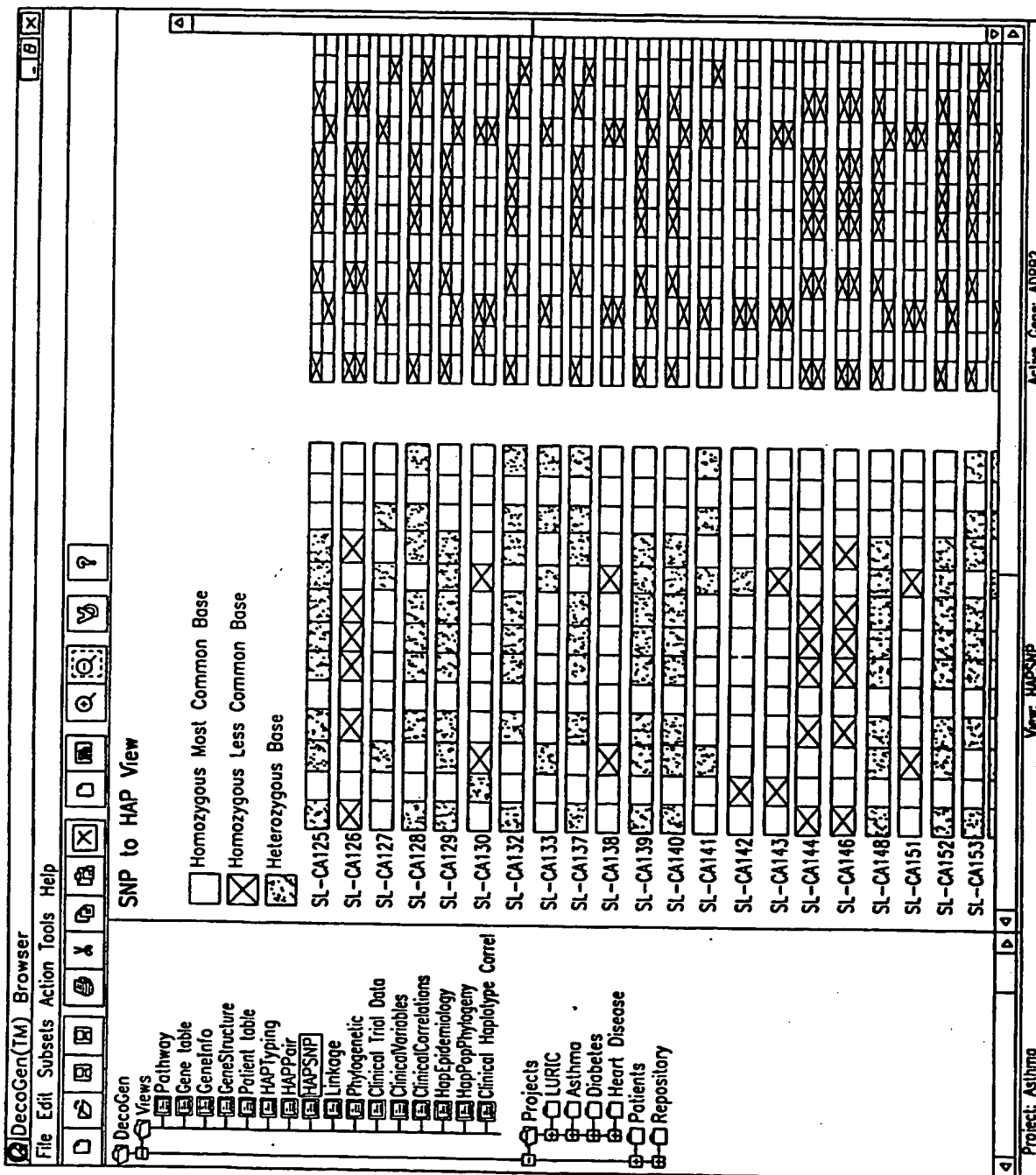
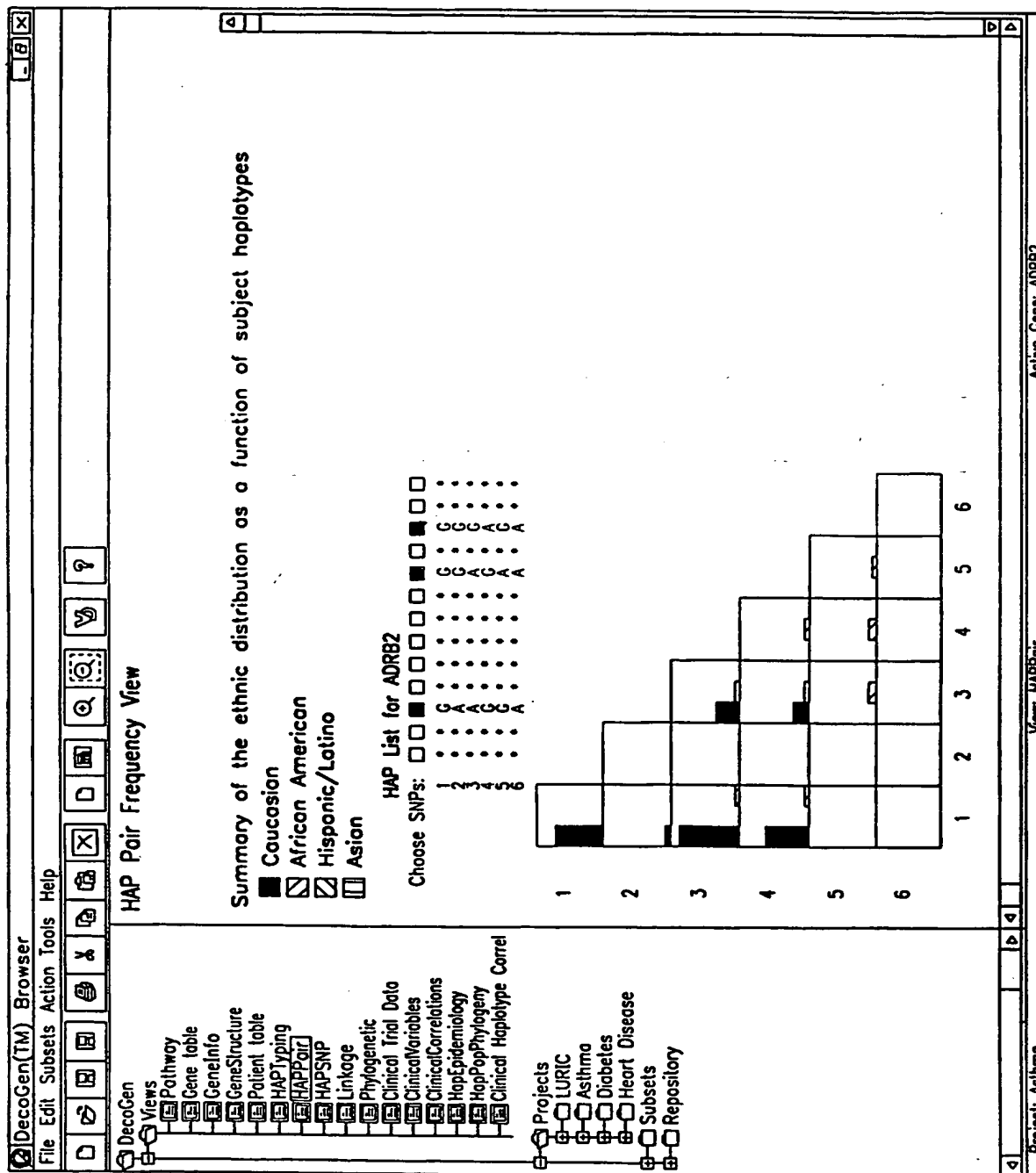


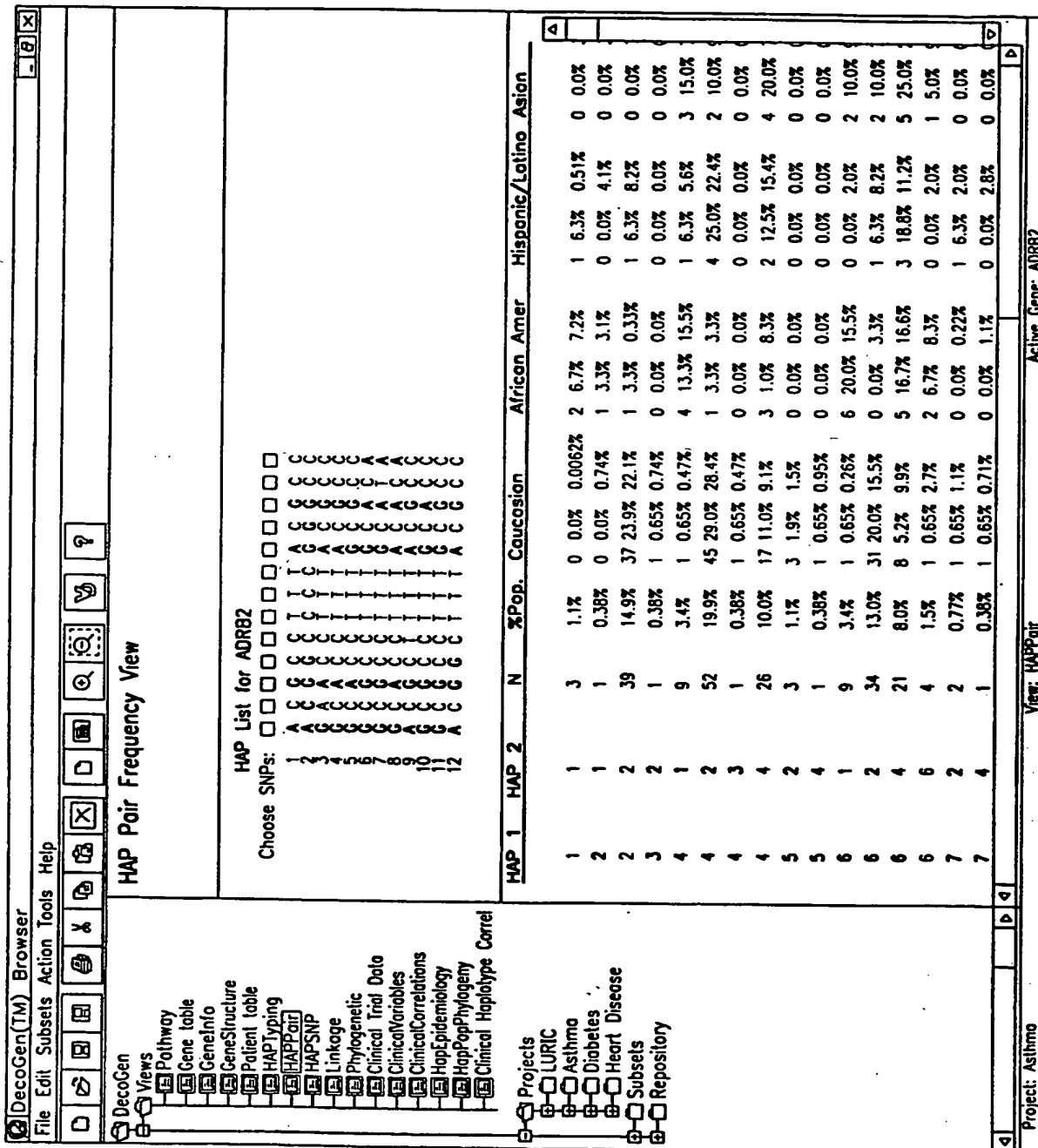
FIG. 3



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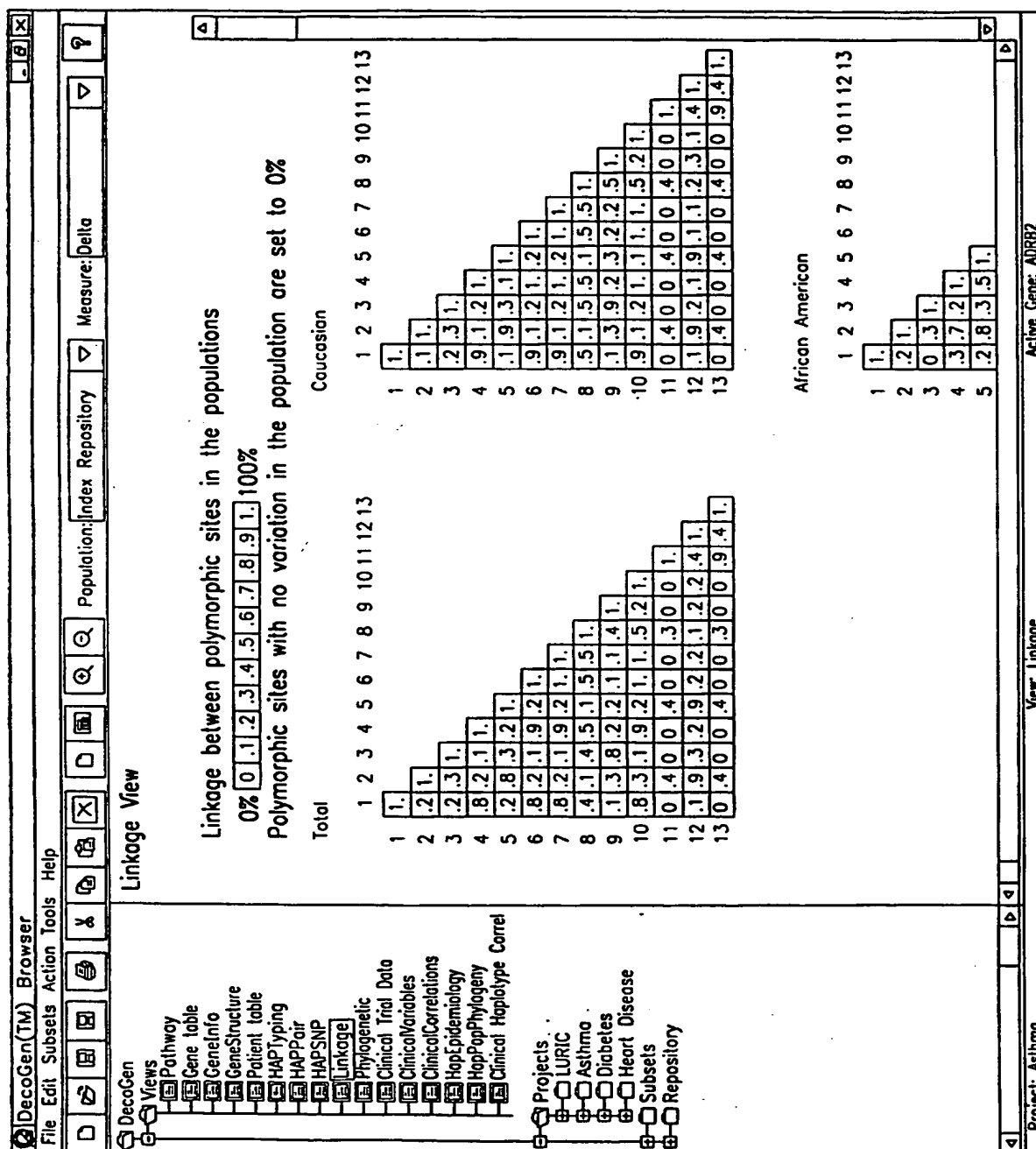
10/019242

FIG. 32



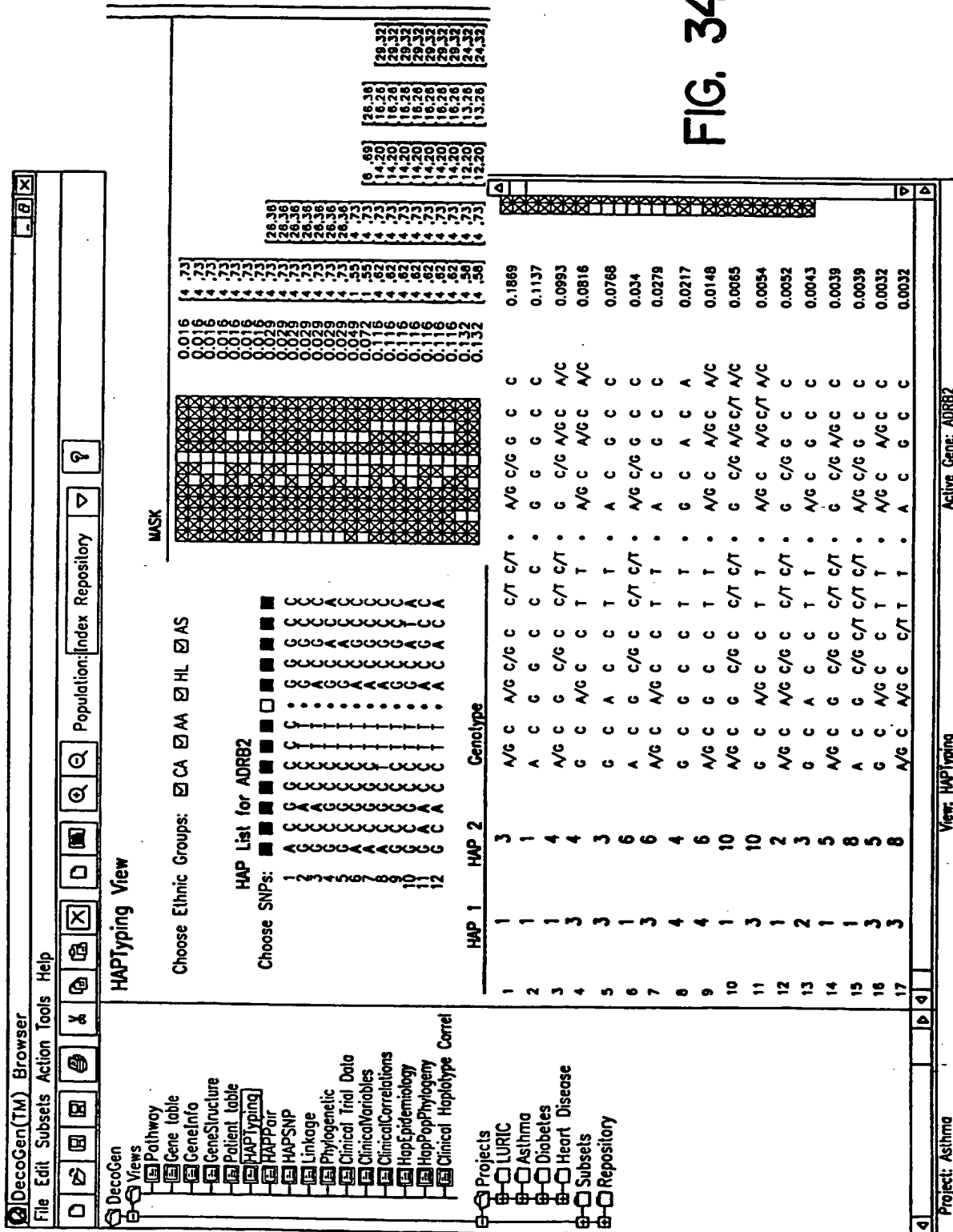
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F/G. 33



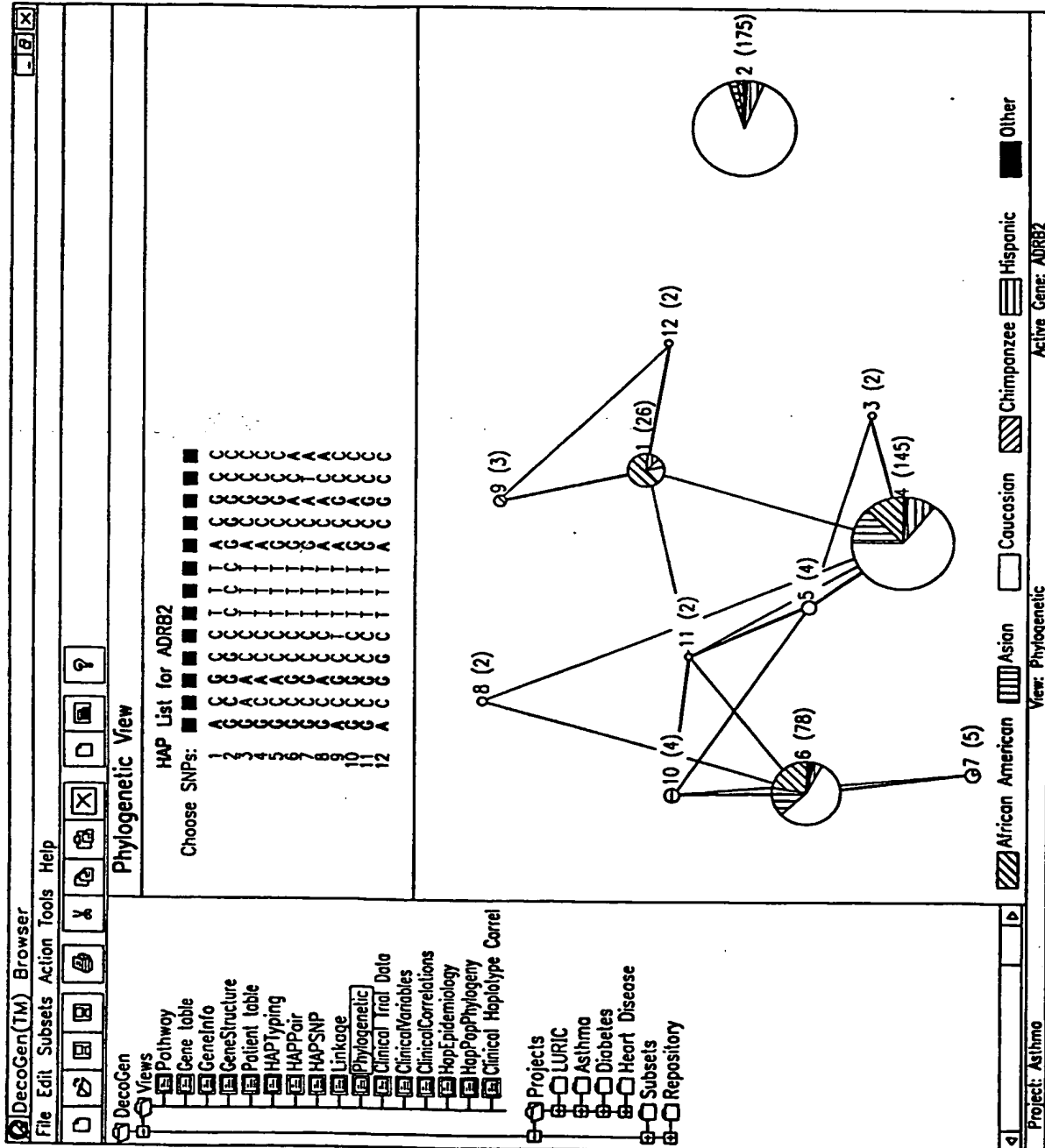
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FIG. 34



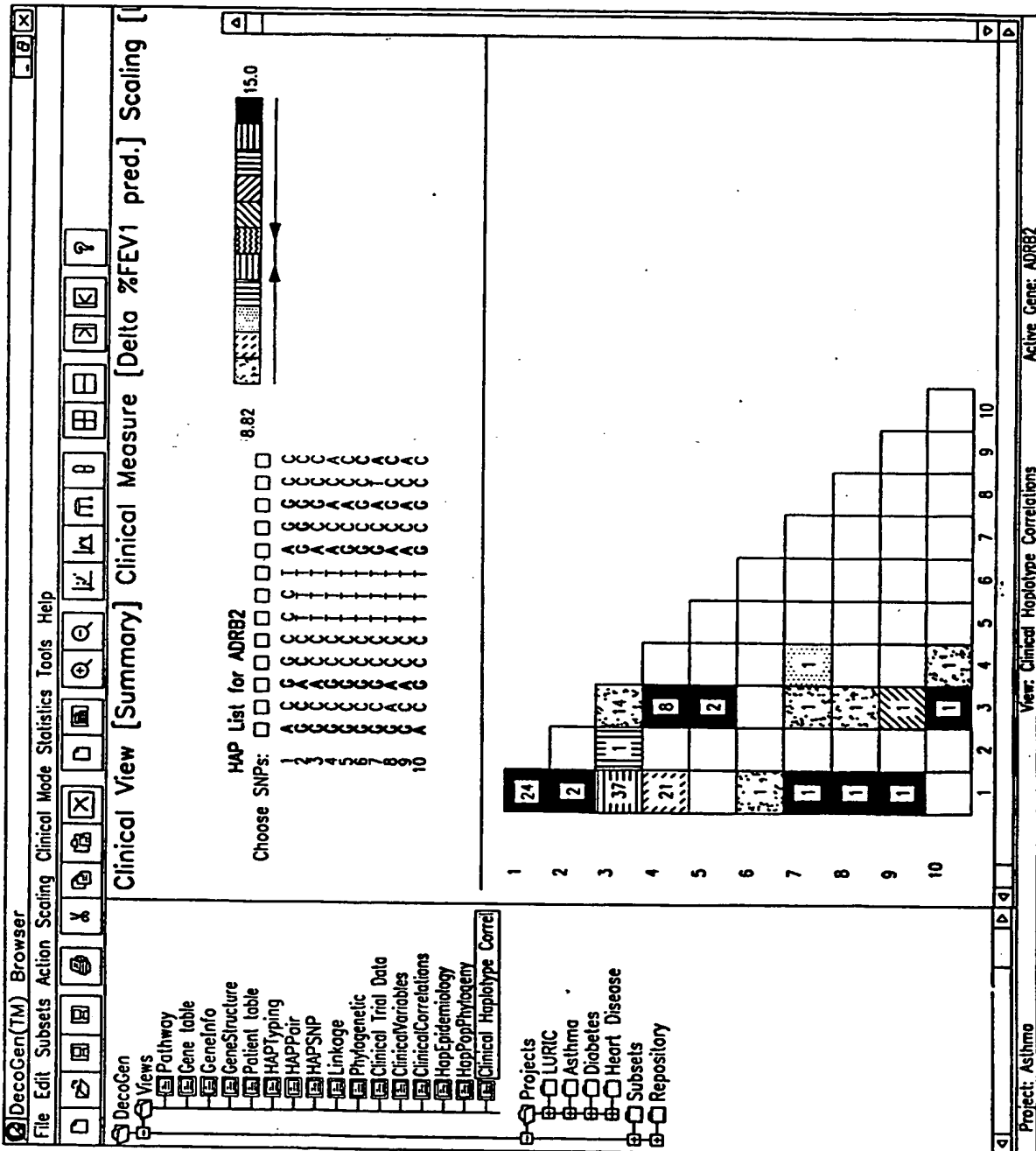
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FIG. 35



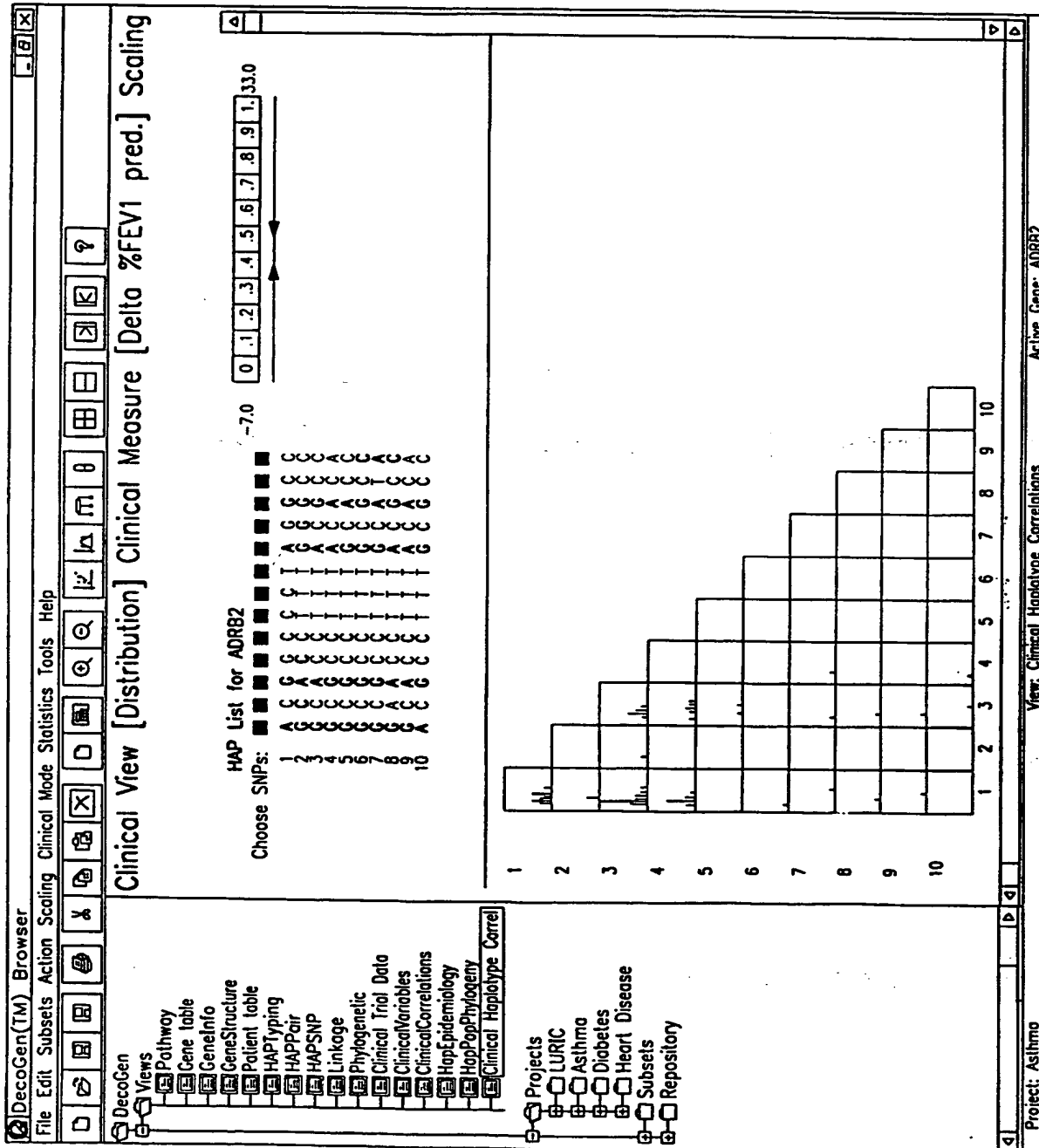
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FIG. 36



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FIG. 37



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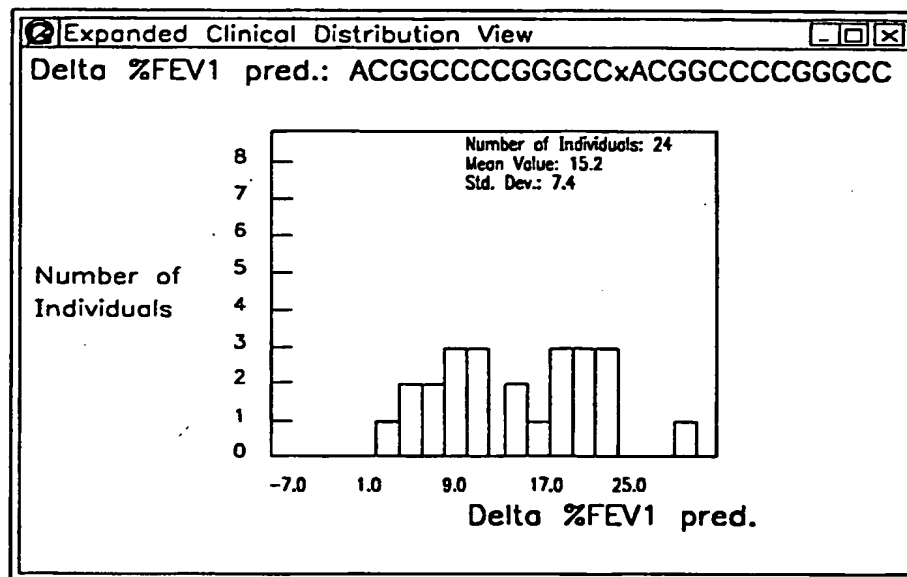


FIG. 38

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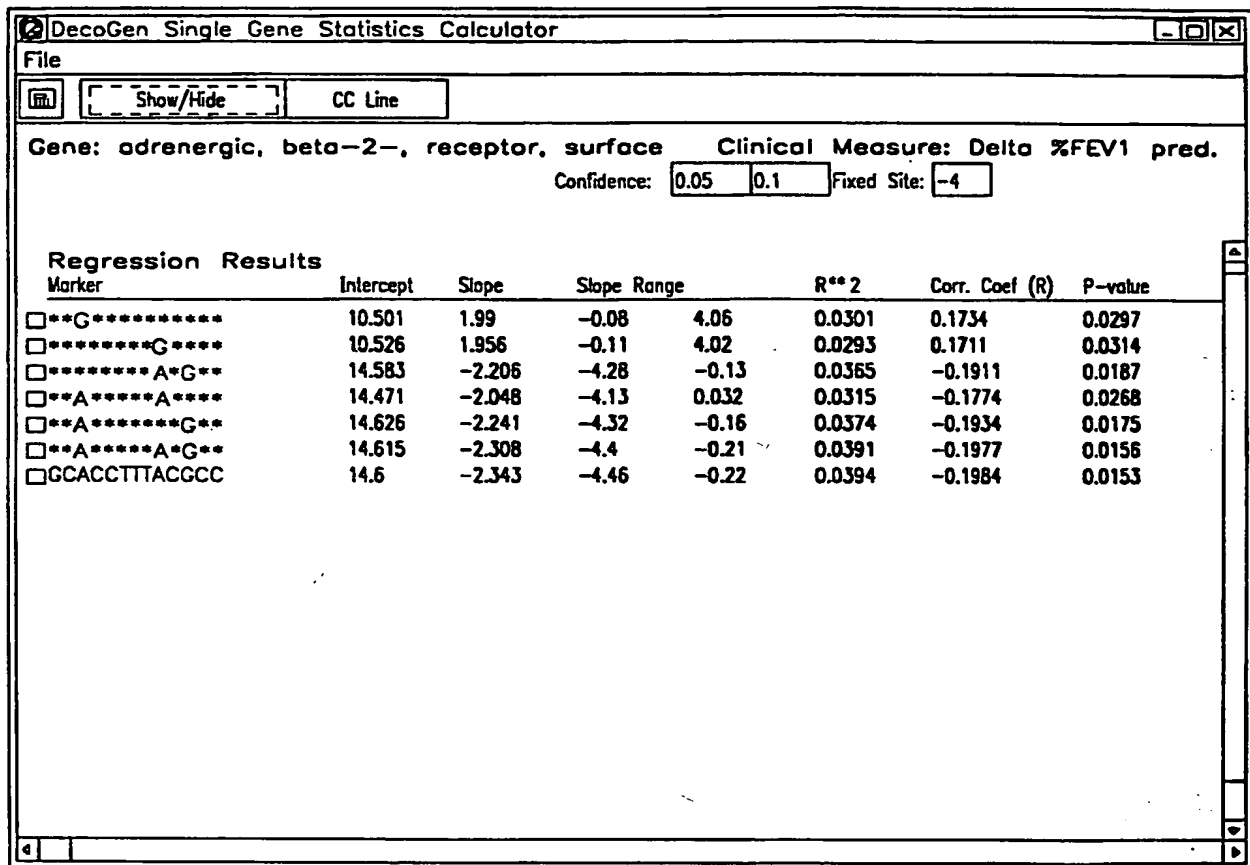


FIG. 39A

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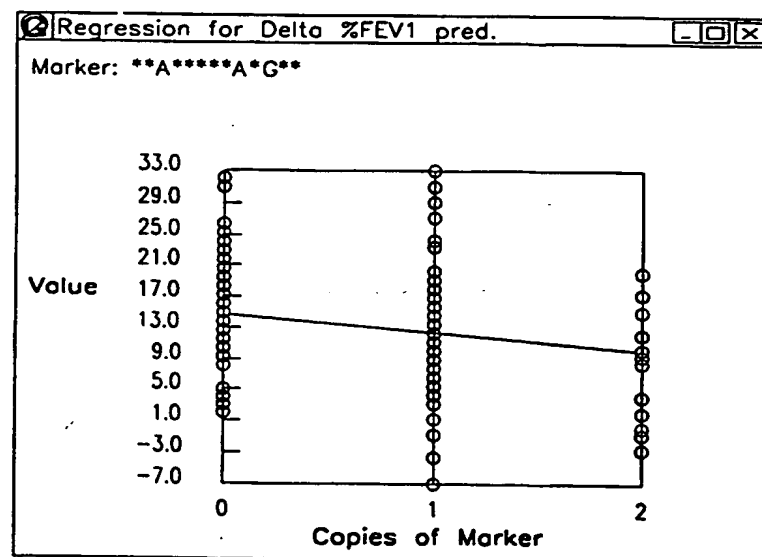
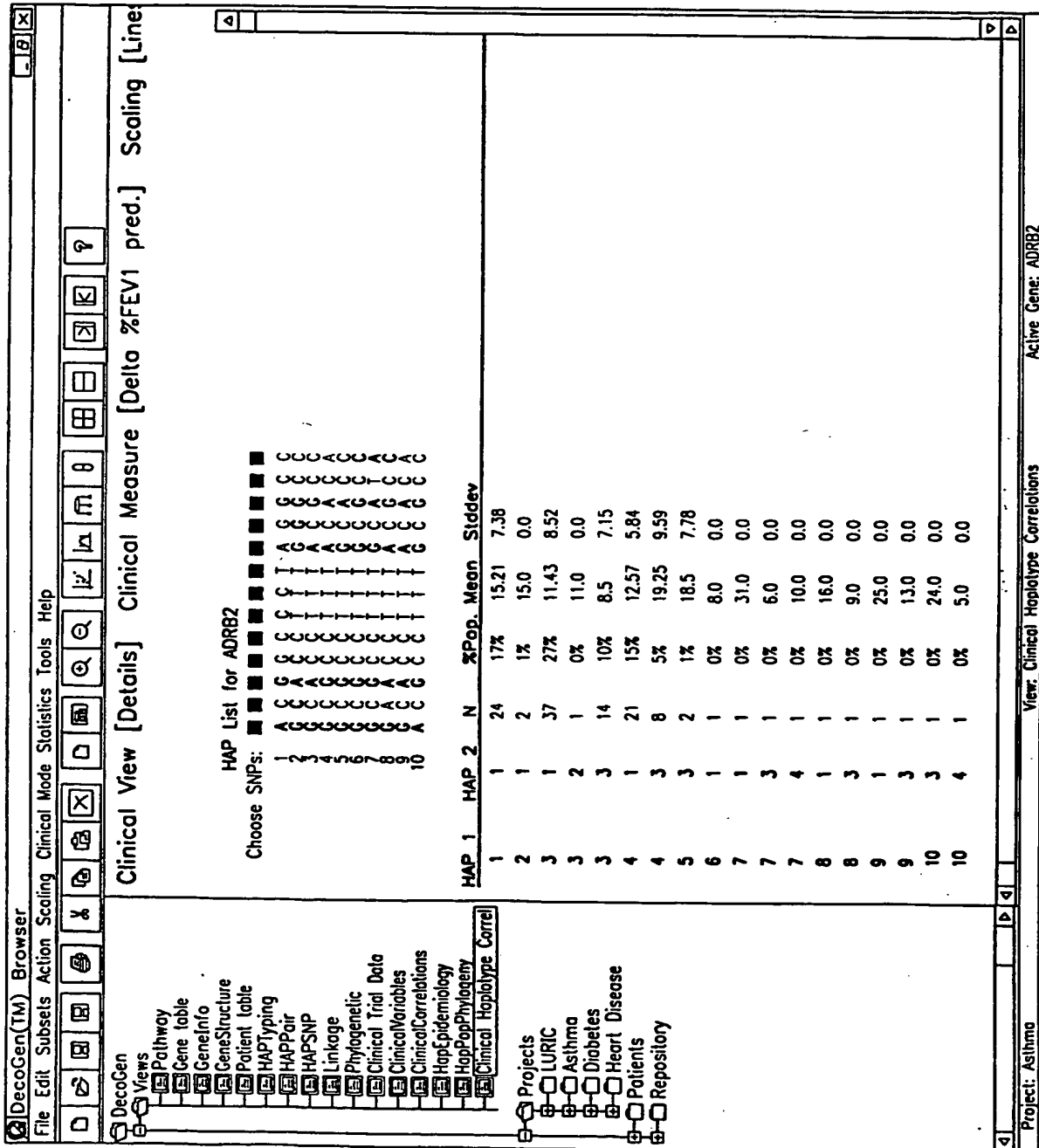


FIG. 39B

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FIG. 40



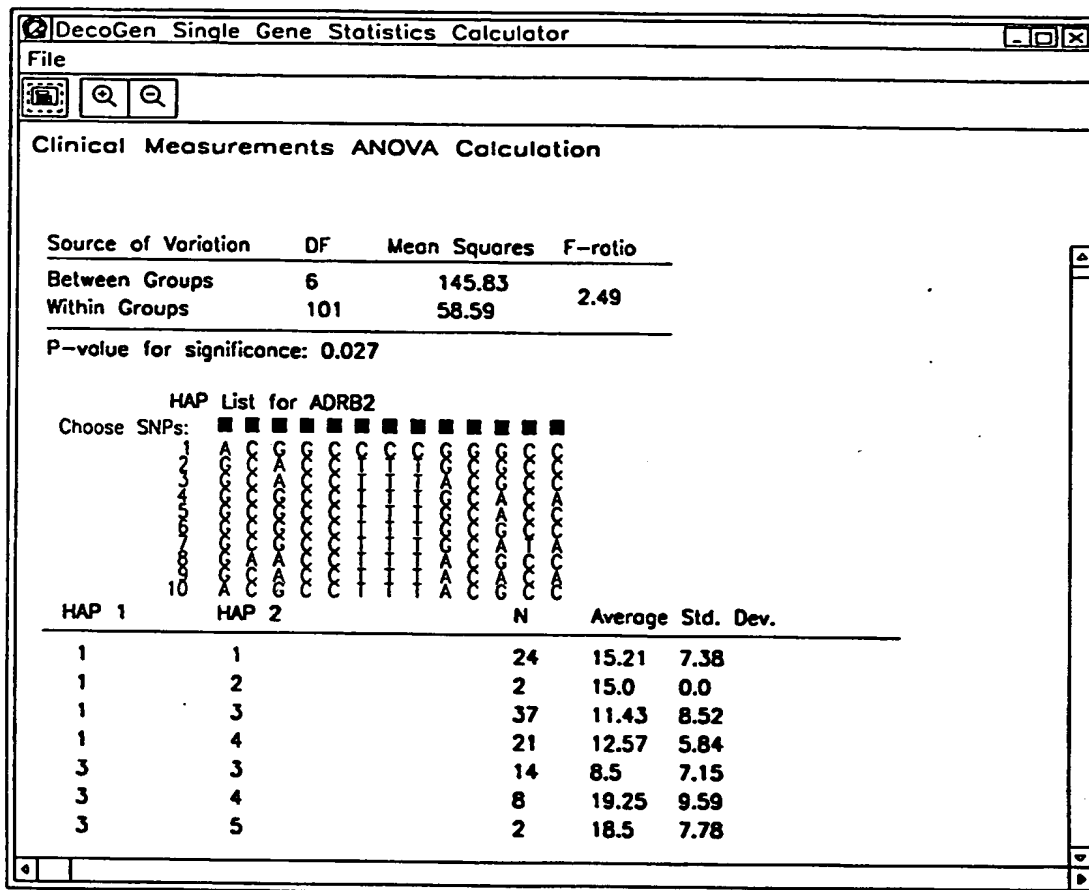
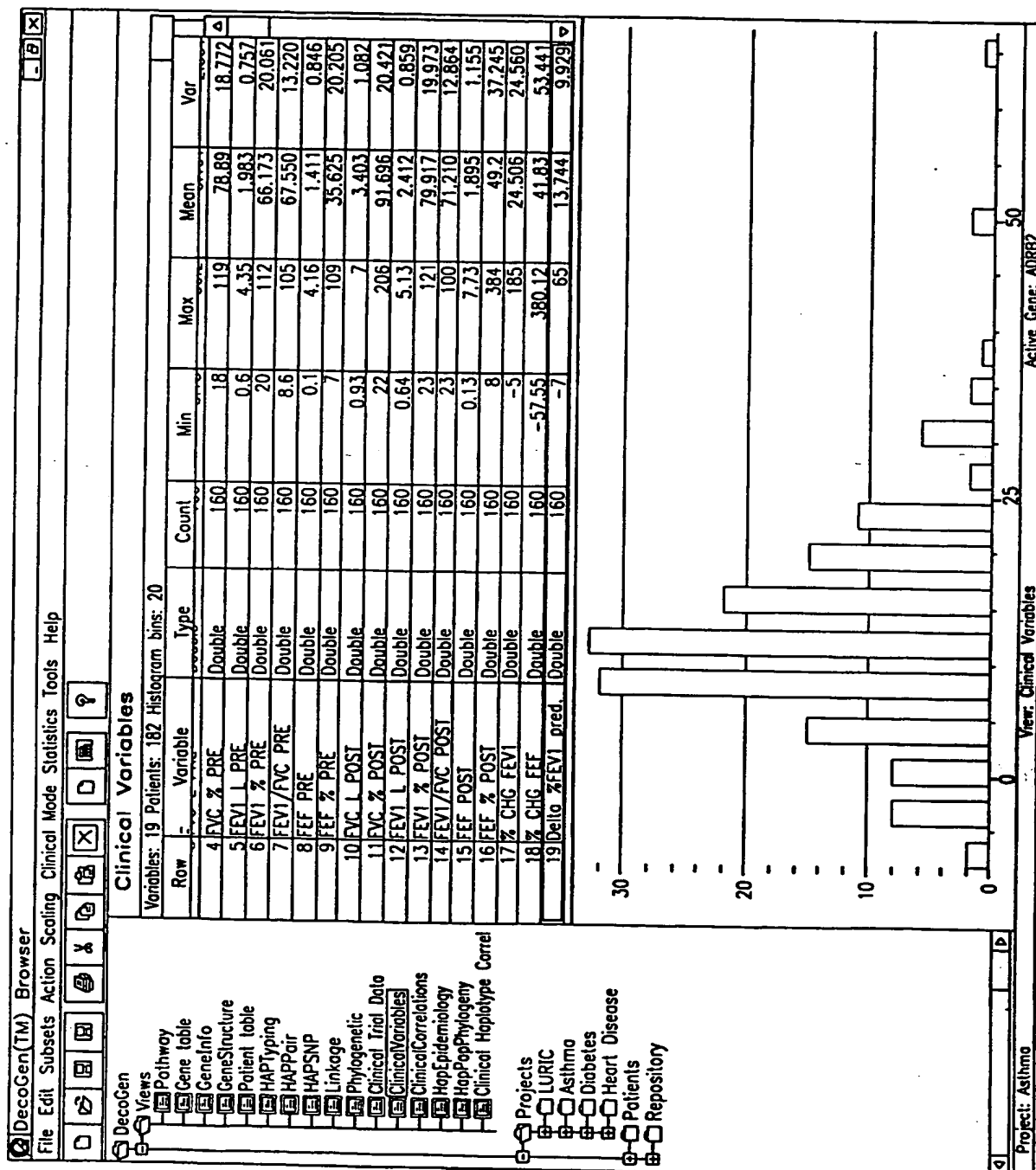


FIG. 41

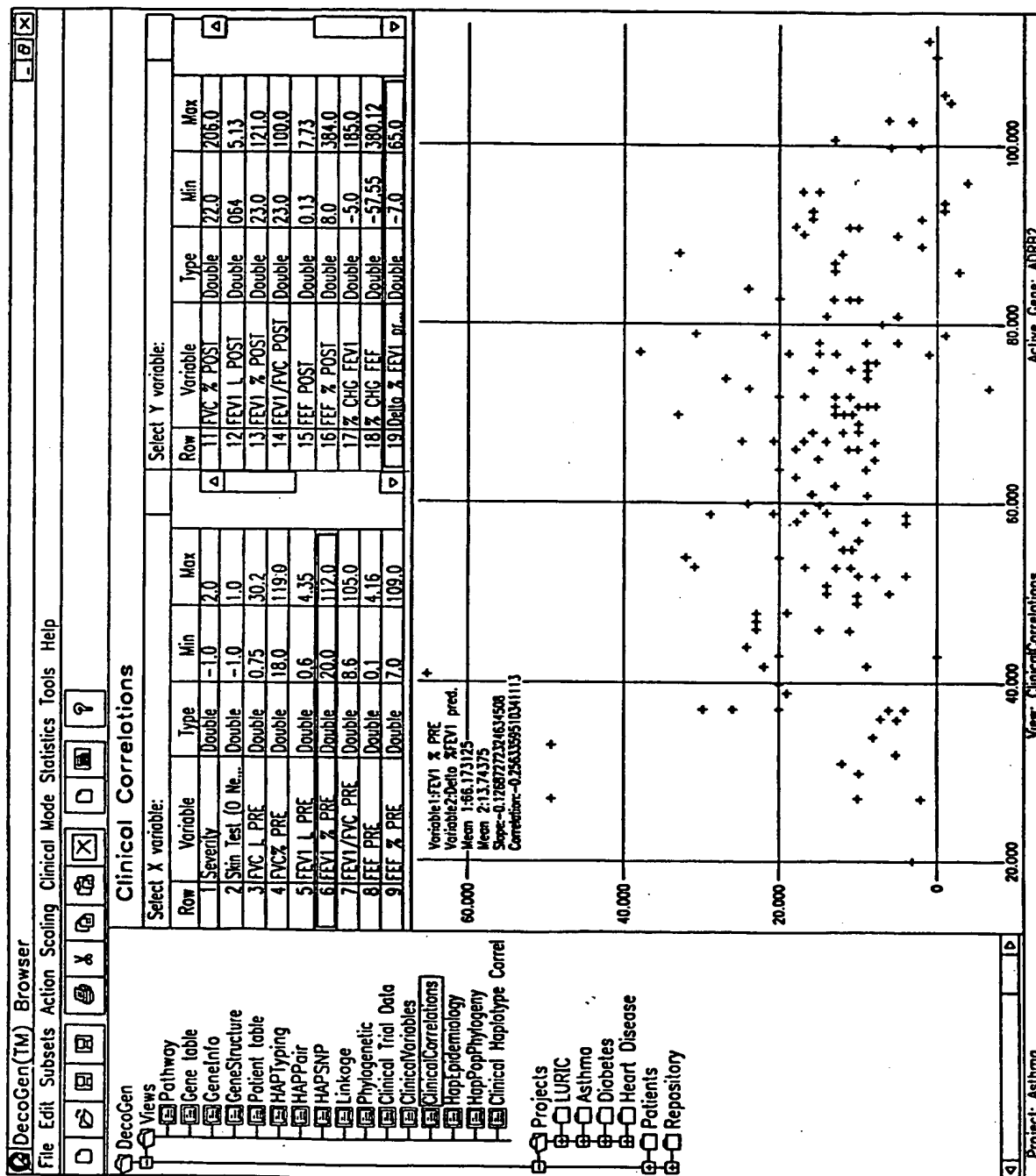
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FIG. 42



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FIG. 43



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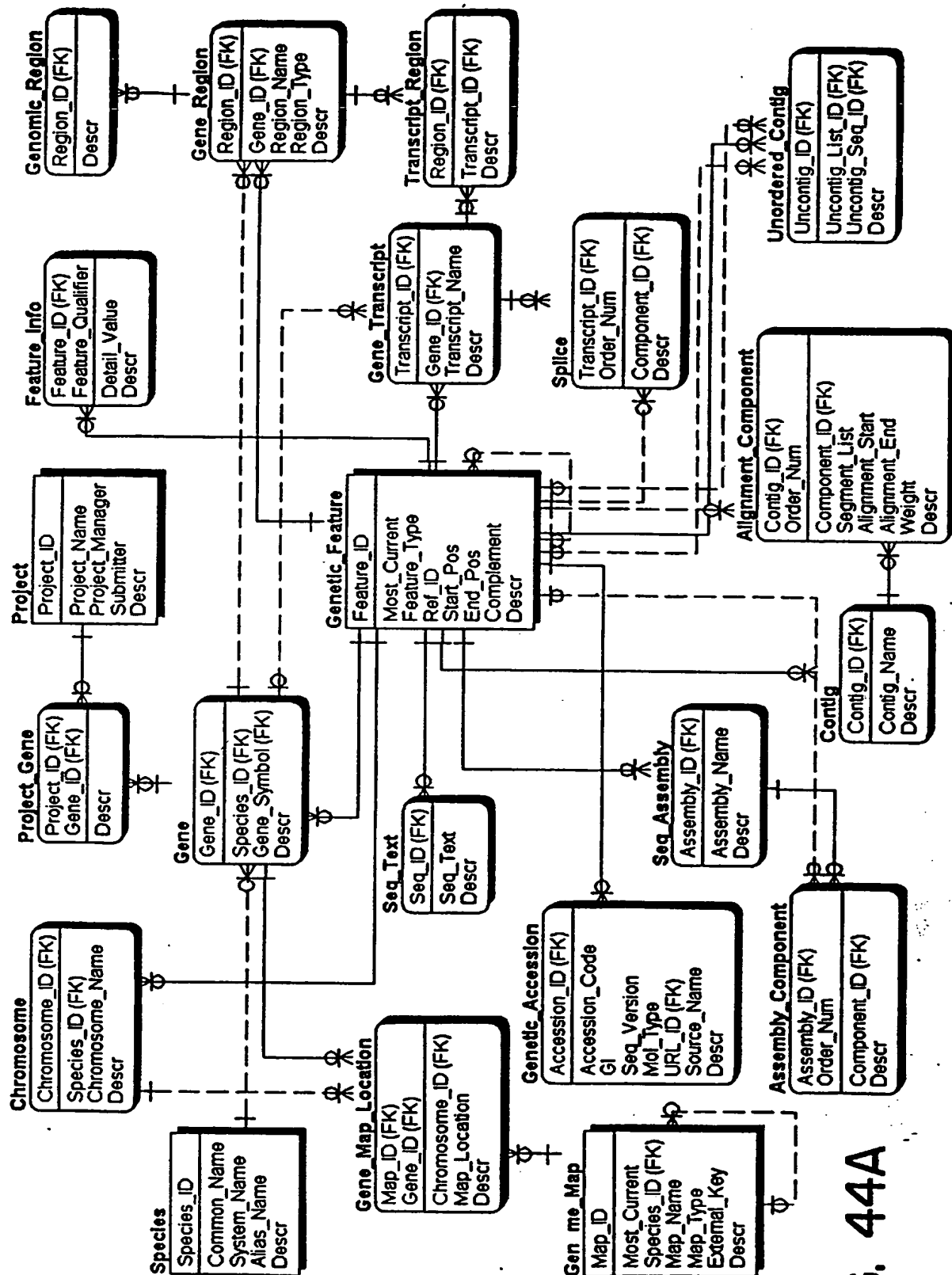


FIG. 44A

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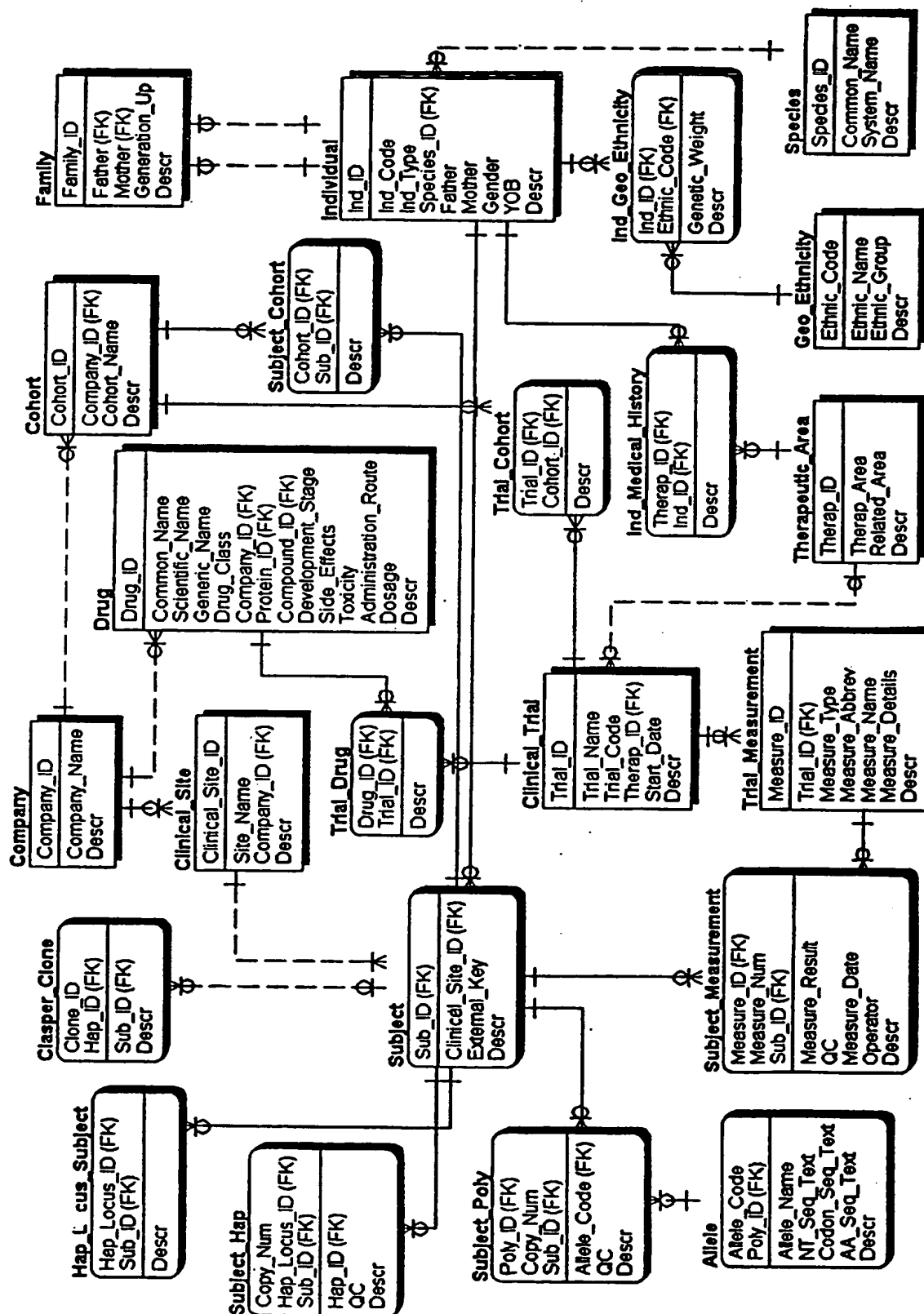


FIG. 44B

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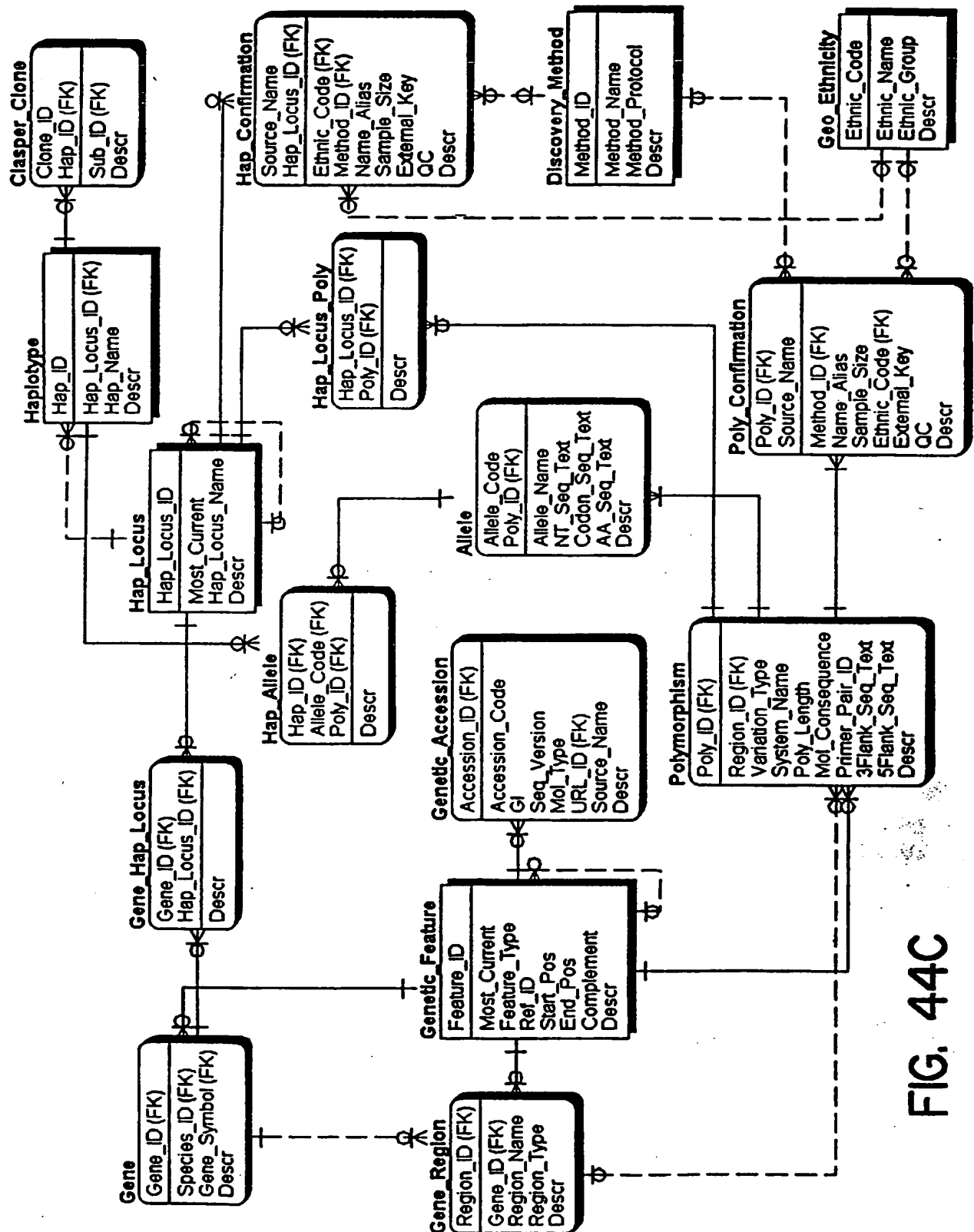
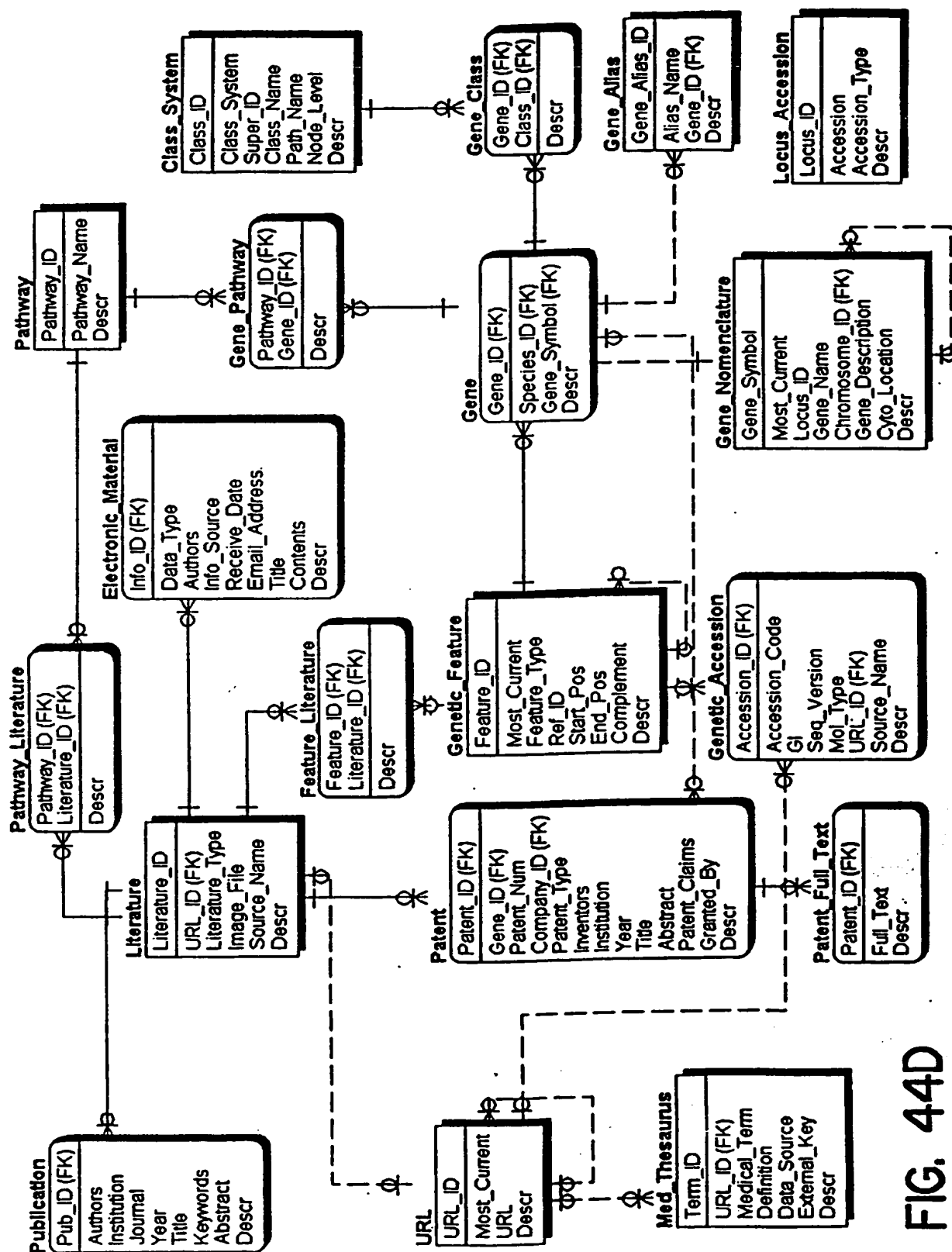
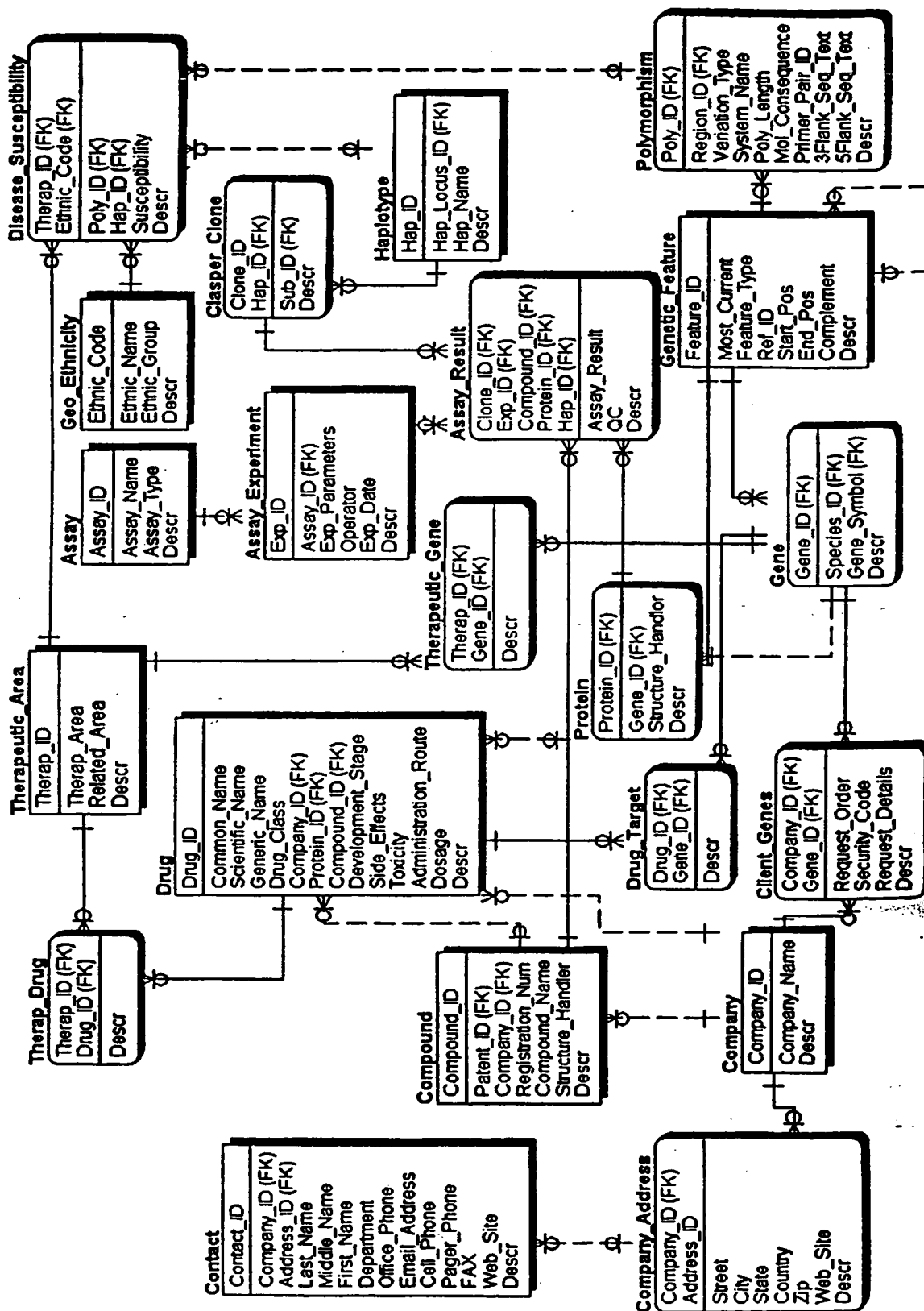
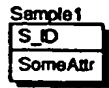


FIG. 44C





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Legend of Figures:

Rectangle Boxes: Tables in the database.



Rounded Boxes: Children tables that depend on their parent tables. This dependency requires that a parent record to be in existence before a child record can be created.

- 2: Identifying parent / child relationship. It depicts the not nullable 1-to-0-or-many relationship.
- 4: Non-identifying parent / child relationship. It represents the nullable 0-or-1-to-many relationship.
- 6: Identifying parent / child relationship. It depicts the not nullable 1-to-1-or-many relationship.
- 8: Non-identifying parent / child relationship. It represents the not nullable 1-to-1-or-many relationship.
- 10: Identifying parent / child relationship. It depicts the not nullable 1-to-exact-1 relationship.
- 12: Non-identifying parent / child relationship. It represents the nullable 0-or-1-to-exact-1 relationship.
- 14: Non-identifying parent / child relationship. It represents the not nullable 0-or-1-to-many relationship.

FIG. 44F

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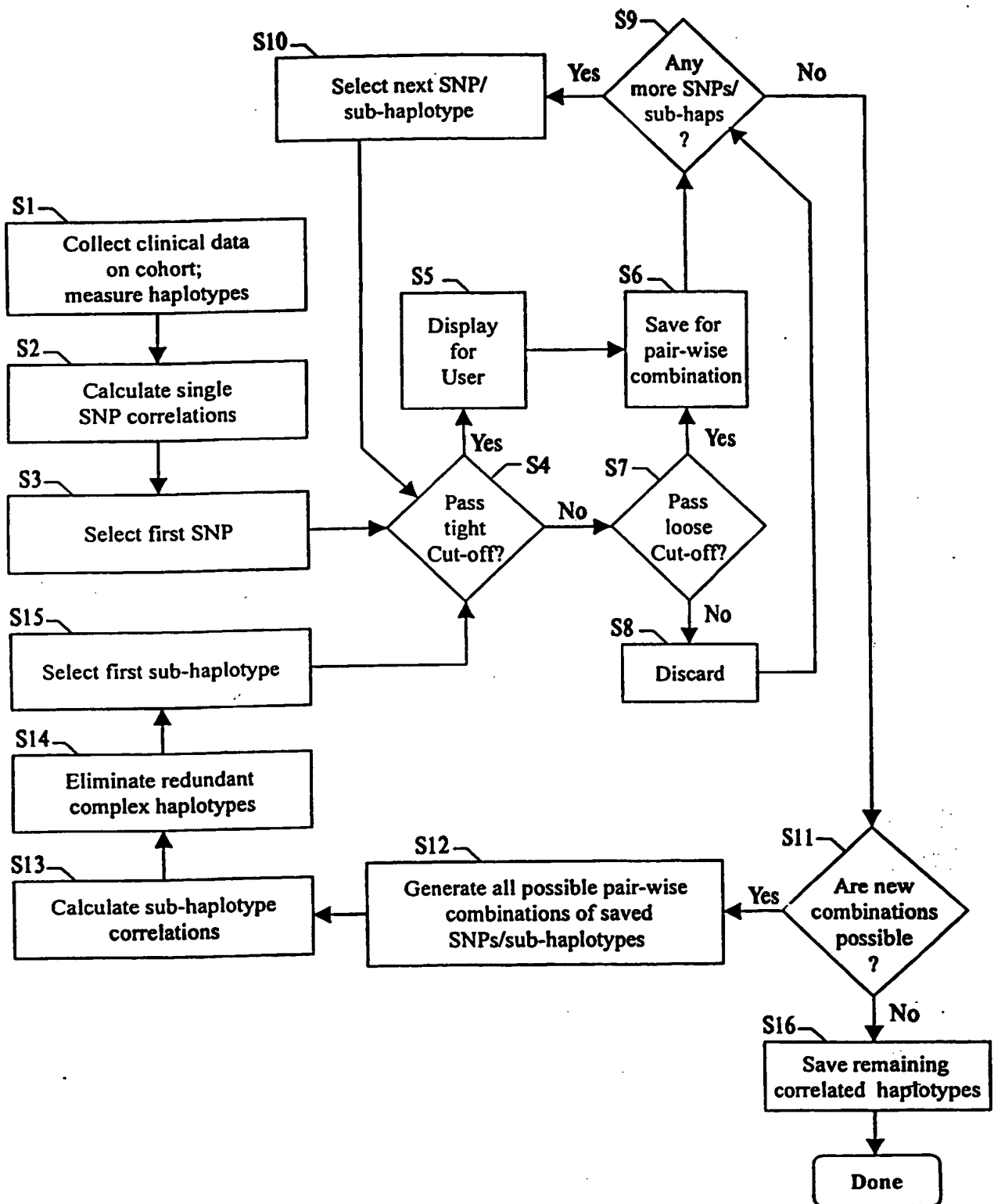


FIG. 45

SUBSTITUTE SHEET (RULE 26)

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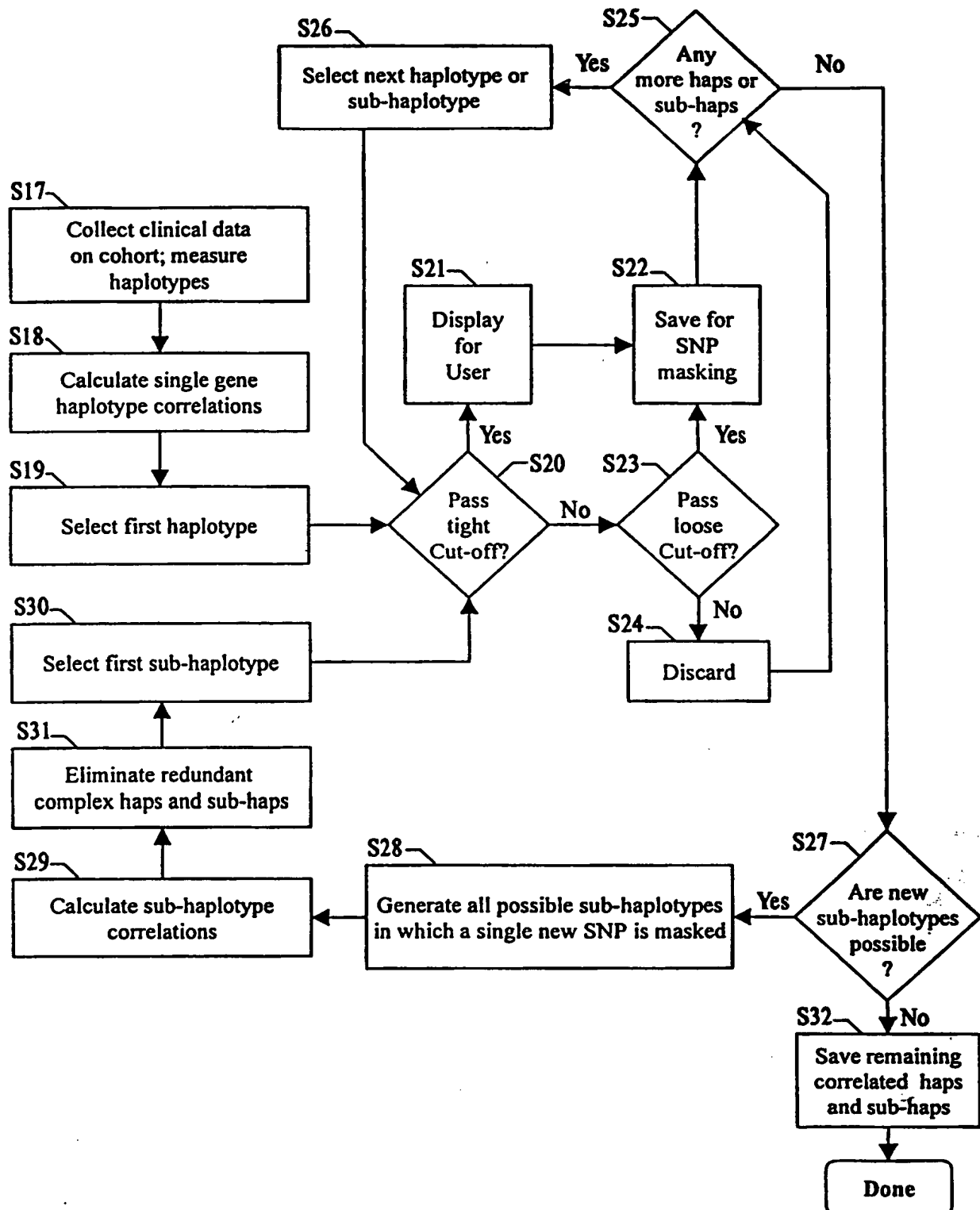


FIG. 46

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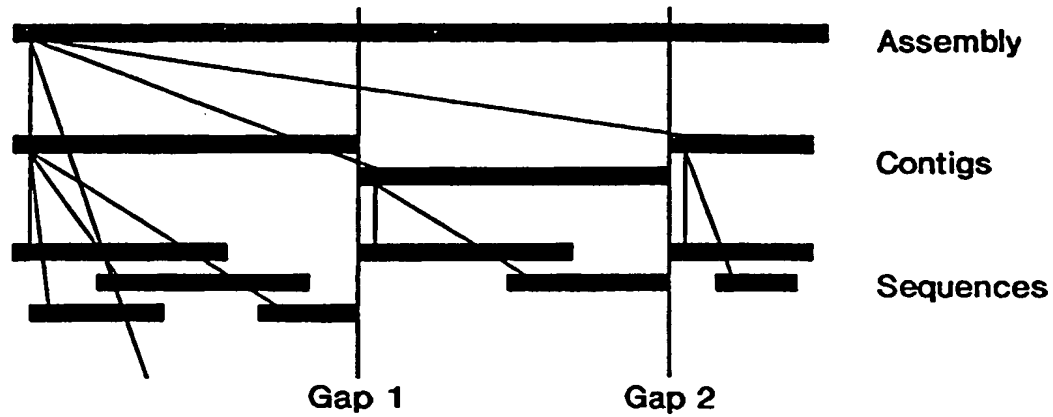


FIG. 47

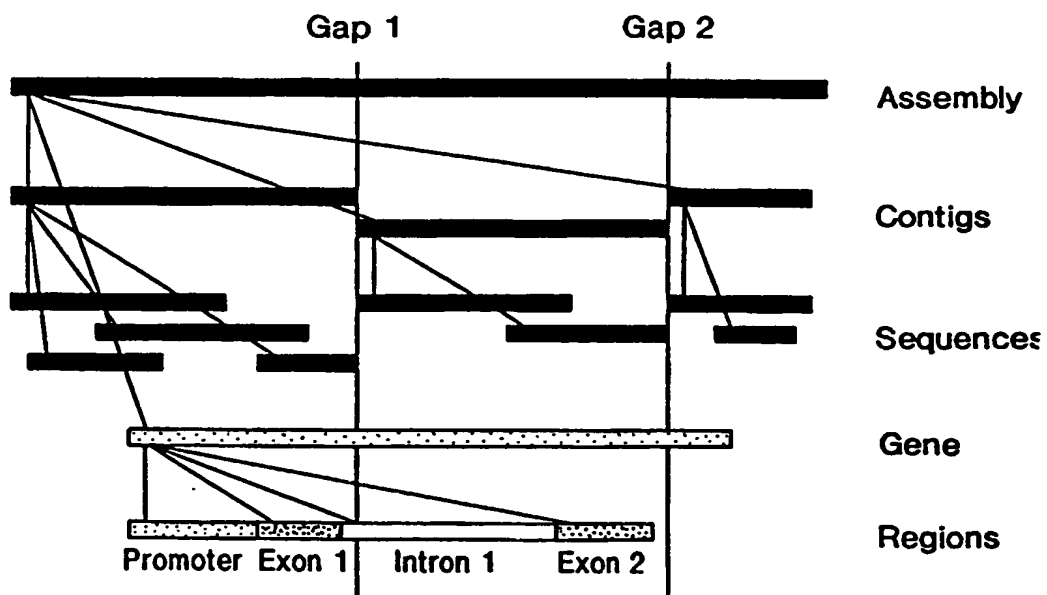


FIG. 48

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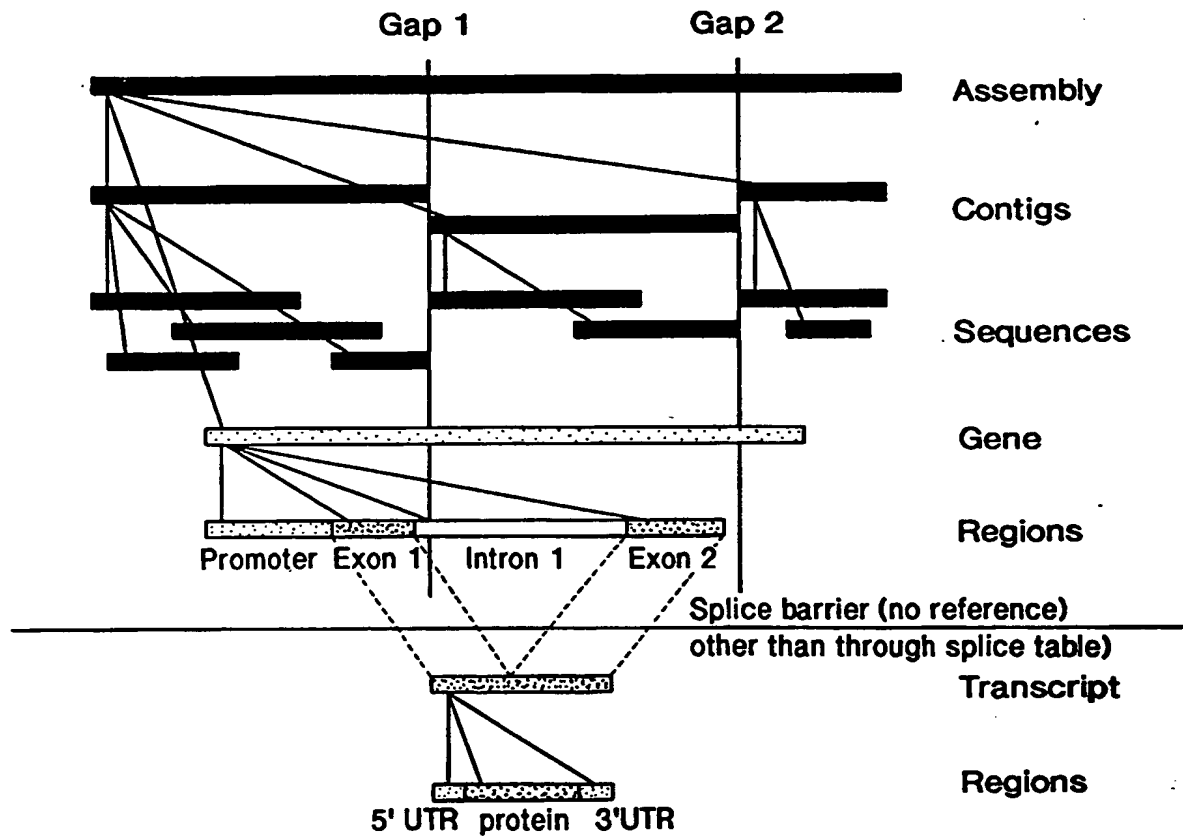


FIG. 49